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POLARITY EFFECTS TRANSMITTED THROUGH A BENZENE NUCLEUS.

THE DIRECTIVE INFLUENCE OF THE TERTIARY-BUTYL-GROUP.

by

Alexander Mackie, B.Sc.(Edin.),A.I.C.

Directed and supervised by J.B.Shoesmith,D.Sc.

Chemistry Department,
University of Edinburgh,

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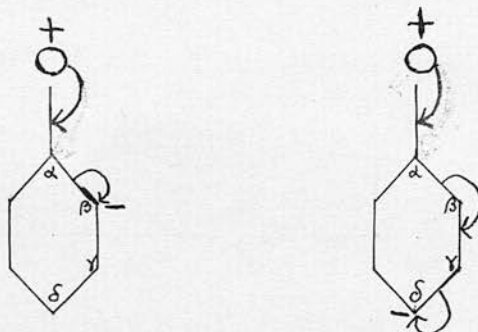
Many investigations have been carried out on the influence of atoms in organic compounds on the reactivity of other atoms in the same molecule. Lapworth and Shoesmith (J.C.S., 1922, 121, 1391), Shoesmith and collaborators (J.C.S., 1923, 123, 2828; 1924, 125, 1312, 2278; 1926, 214, 2832; 1927, 1768) have investigated influences governing reactivity in substituted halogenated benzenoid derivatives with a view to discovering how far reactivity is determined by (1) general influences, where the introduction of an atom or group affects the reactivity of the molecule as a whole, (2) alternating influences, which are responsible for alternation of reactive positions, and (3) spatial and steric influences, which are generally apparent in ortho-compounds and α -substituted aliphatic compounds, (compare Flürscheim, J.C.S., 1909, 95, 718; Lapworth, Mem. Manchester Phil. Soc., 1920, 64, No. 3; Kermack and Robinson, J.C.S., 1922, 121, 428; Lapworth and Shoesmith, loc. cit.; Robinson, Ann. Reports, 1922, 19, 98), since the reactivity of any atom in an organic molecule is governed by these factors.

Particular attention has been directed to the second of these, and the experimental results obtained were in many cases predicted by, and have substantiated the principle of induced alternate polarities formulated/

formulated by Lapworth (Mem. Manchester Phil. Soc., 1920, 64, 11, 1; J. C. S., 1922, 121, 416), which postulates the production of reactive positions in an organic molecule owing to the presence of a "key-atom". The "key-atom" induces alternately, similar polarities on atoms in a chain or ring and is denoted by a dot attached to its polar sign. The principle may be regarded as of fundamental importance and "as the basis of the future development of organic chemistry" (compare van Duin, Z. physikal. Chem., 1927, 130, 364). The reason why certain atoms, notably oxygen, should be potent "key-atoms" in an organic molecule, is as yet somewhat obscure, but it is certainly not due to the negativity or positivity of an atom, as usually regarded, since, when fluorine is compared with oxygen it is found that the latter is the more powerful "key-atom", and it appears to be due largely to the conjugation of the oxygen atom with the atoms through which the influence is transmitted.

This theory put forward by Robinson (Chem. and Ind., 1925, 44, 456) explains the phenomena of substitution in a benzene nucleus containing a hydroxyl-group. The oxygen atom is a source of electrons, one of which moves to the α -carbon atom and the remaining electrons of the nucleus undergo a rearrangement which results in the β - and δ -carbon atoms, that is the ortho- and para-positions, becoming negatively/

negatively charged, the condition necessary for attack by reagents such as nitric acid and benzene diazonium chloride, etc. This is seen from the figure:



The theory has been remarkably fruitful in explaining the various phenomena met with in benzene substitution.

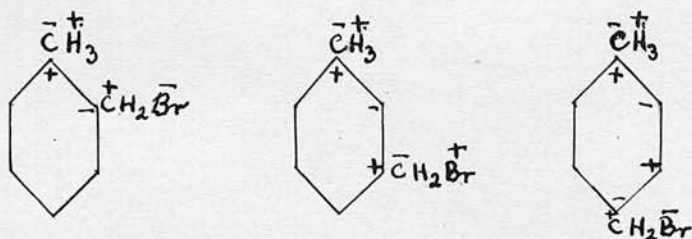
The similarity of the methyl- to the hydroxyl-group as regards directive influence suggests that the carbon atom of the methyl-group should be similar to the oxygen of the hydroxyl-group. The earlier theory of Lapworth postulated that the hydrogen of the methyl-group would act as a positive "key-atom", whilst in accordance with the later theory of Robinson (J.C.S., 1926,401), the methyl-group is to be regarded as an "electron source".

It was from the point of view of testing the truth of the theory of induced alternate polarities that Shoesmith and Slater (J.C.S., 1924, 125, 2278) investigated the reactivity of the bromine in the isomeric ω -bromo-xylenes in which the directive influence of the methyl-group is manifest and discovered/

discovered that as far as the behaviour of those compounds were concerned, the suggestions of Lapworth were absolutely correct. Thus the order of ease of hydrolysis of these compounds, in which a negatively induced bromine atom in the ortho- and para-isomerides should be more easily removed than the positively induced bromine atom in the meta-compound, was actually ortho and para > meta, whilst when the bromides were allowed to react with hydrogen iodide, that is a reagent chosen to show the "positive" nature of the bromine, the order of ease of removal was reversed. The expected polarity of the bromine atom in these compounds may be seen from the figures below and the reactions employed to demonstrate the differences were (1) $R.CH_2\bar{B}r + \overset{+}{H}\overset{-}{OH} \longrightarrow R.CH_2OH + HBr$ and (2) $R.CH_2\overset{+}{B}r + \overset{+}{C}H\overset{-}{I} \longrightarrow R.CH_3 + IBr$

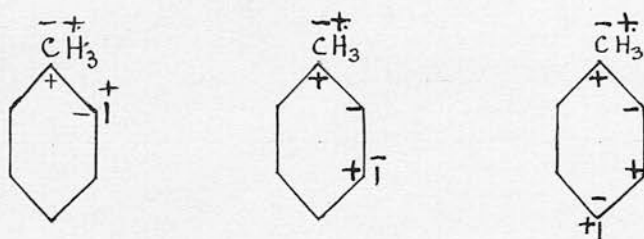
$$I Br + HI \longrightarrow I_2 + HBr$$

The liberated iodine in the latter case was a measure of the reduction which had taken place.

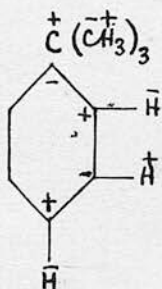


The influence of the methyl-group was also apparent in/

in the manner in which the isomeric iodo-toluenes behaved with hydrogen iodide. In this case, the halogens are one place nearer the "key-atom" than in the ω -bromo-xylenes, and it was found that the ortho- and para-isomerides were reactive, whilst the meta-derivative was very slowly reduced.



There are however several exceptions to the simple polarity rule, one of which is the nitration of tertiary-butyl-benzene, where the substituent enters the para-position (Malherbe, Ber., 1919, 52, 319) to a preponderating degree. The "key-atoms", that is the hydrogen atoms, since they are one place removed from the benzene ring as compared with those in toluene, would be expected to bring about meta substitution.

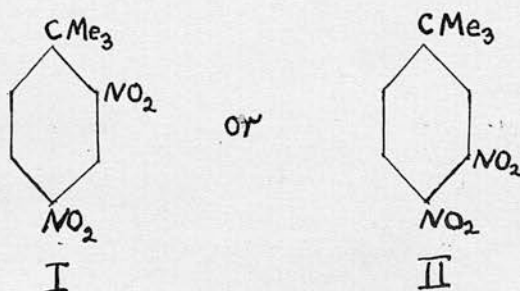


The formation of a p-nitro-compound may however be due to a large steric effect of the tertiary-butyl-group/

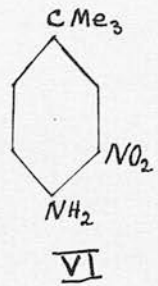
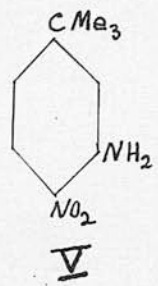
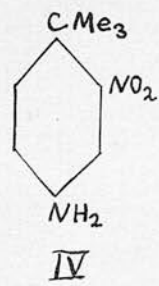
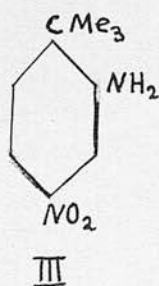
group (compare Ingold, Ann. Reports, 1926, 23, 141; Vorländer, Ber., 1919, 52, 274) which causes all substituents to enter the nucleus as far as possible away from the group already present in the molecule or a large general influence which pushes all the electrons to the para-position and hence there would be no alternating effect in the general sense of the term. The methods used in the investigation of the directive power of the methyl-group would readily show the presence of the alternating influence and therefore the following compounds have been prepared and the lability, that is the ease of replacement of the halogens in them, investigated ;(1) the isomeric iodo-tertiary-butyl-benzenes of the general formula, $\text{Me}_3\text{C} \cdot \text{C}_6\text{H}_4 \cdot \text{I}$ and (2) m- and p-tertiary-butyl-benzyl bromides, $\text{Me}_3\text{C} \cdot \text{C}_6\text{H}_4 \cdot \text{CH}_2\text{Br}$. The isomeric tertiary-butyl-benzoic acids, $\text{Me}_3\text{C} \cdot \text{C}_6\text{H}_4 \cdot \text{COOH}$, the last of the series, were prepared in order to trace any regularities which might appear in their dissociation constants, since this is one of the properties influenced by substituent groups.

The method of preparing the iodo-tertiary-butyl-benzenes involved the isolation of the corresponding amines, and whilst the details concerning the meta- and para-isomerides were available, it is noteworthy that no ortho-derivative of tertiary-butyl-benzene whose constitution could be regarded as having/

having been determined had hitherto been prepared. Seńkowski (Ber., 1890, 23, 2414) described a compound, separated from a nitration mixture of o- and p-nitro-tertiary-butyl-benzenes, as the o-nitro-derivative, but he put forward no proof of the constitution. This was probably due to the difficulty of converting the compound to o-nitro-benzoic acid and which was also encountered in the present research, but from the manner in which it was finally prepared and its subsequent reduction to the amino-compound, it has been possible to show that Seńkowski was correct. p-Nitro-tertiary-butyl-benzene, which was proved by Malherbe (loc.cit.) to be the p-nitro-derivative, since on oxidation it gives p-nitro-benzoic acid, was further nitrated and gave dinitro-tertiary-butyl-benzene. This compound must have the constitution I or II.



On reduction with ammonium hydrogen sulphide, the dinitro-compound gave a nitro-amine, m.p. 54.5°-55.5°, which must have the constitution III, IV, V or VI.



Compound (VI) (Ber., 1887, 20, 3254), m.p. 106.5°, has been described by Gelzer.* The nitroamine prepared from the dinitro-compound must therefore be either III, IV or V. By elimination of the amino-group from III or V, p-nitro-tertiary-butyl-benzene would result, whilst from IV, the ortho-nitro-derivative would be formed. The amino-derivative obtained on reduction of this nitro-compound gave an acetamino-derivative of m.p. 161° - 162°. p-Acetamino-tertiary-butyl-benzene has m.p. 169°, whilst a mixture of the two had m.p. 127.5° - 130.5°. This acetamino-derivative must therefore be o-acetamino-tertiary-butyl-benzene and hence the nitroamino- and dinitro-compounds have the constitutions represented by formulae IV and I respectively.

This point is of importance since it shows that the ortho- and para-positions are attacked in direct nitration but not the meta.

The/

* This compound described by Gelzer as a derivative of isobutyl-benzene is a tertiary-butyl-benzene derivative. Gelzer (Ber., 1888, 21, 2950) also describes a compound of m.p. 124° as 2-nitro-3-amino-isobutyl-benzene (in reality a tertiary-butyl-benzene derivative). This is quoted in Richter's Lexikon as the 3-amino-4-nitro-derivative, which it probably is, but since there is a doubt as to its constitution, it is not referred to in the present thesis.

The isomeric iodo-tertiary-butyl-benzenes were prepared as described later and submitted to the action of hydriodic acid in glacial acetic acid solution at 25° (compare Shoesmith and Slater, loc. cit., p. 2281), when it was discovered that the ortho-compound was very reactive, the para reactive but less so than the ortho-derivative and the meta not affected. The same order of reactivity was observed when the iodo-compounds were acted upon by hydriodic acid at 100° . The graphs illustrating these results are given in Figures I and II.

Figure I.

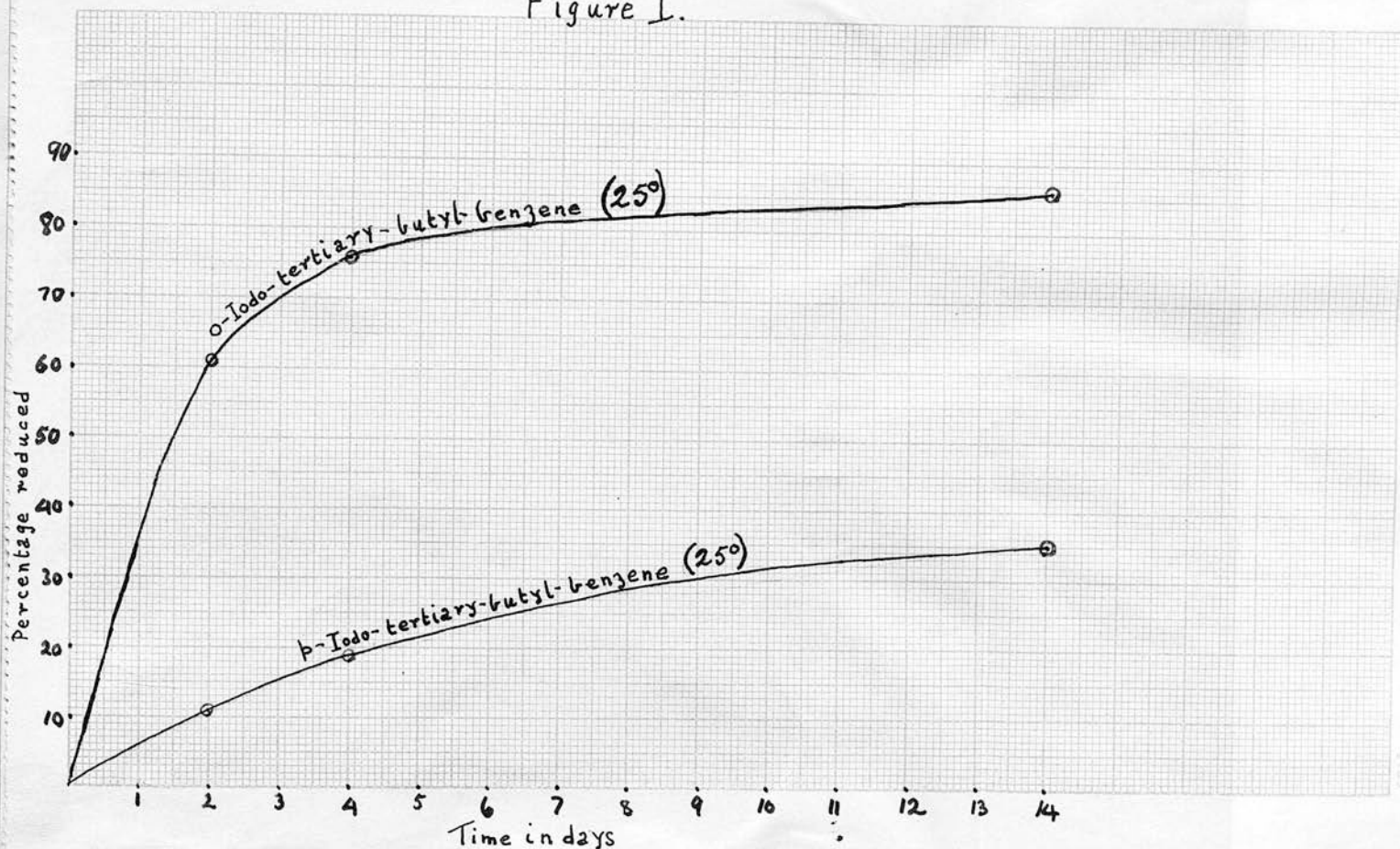
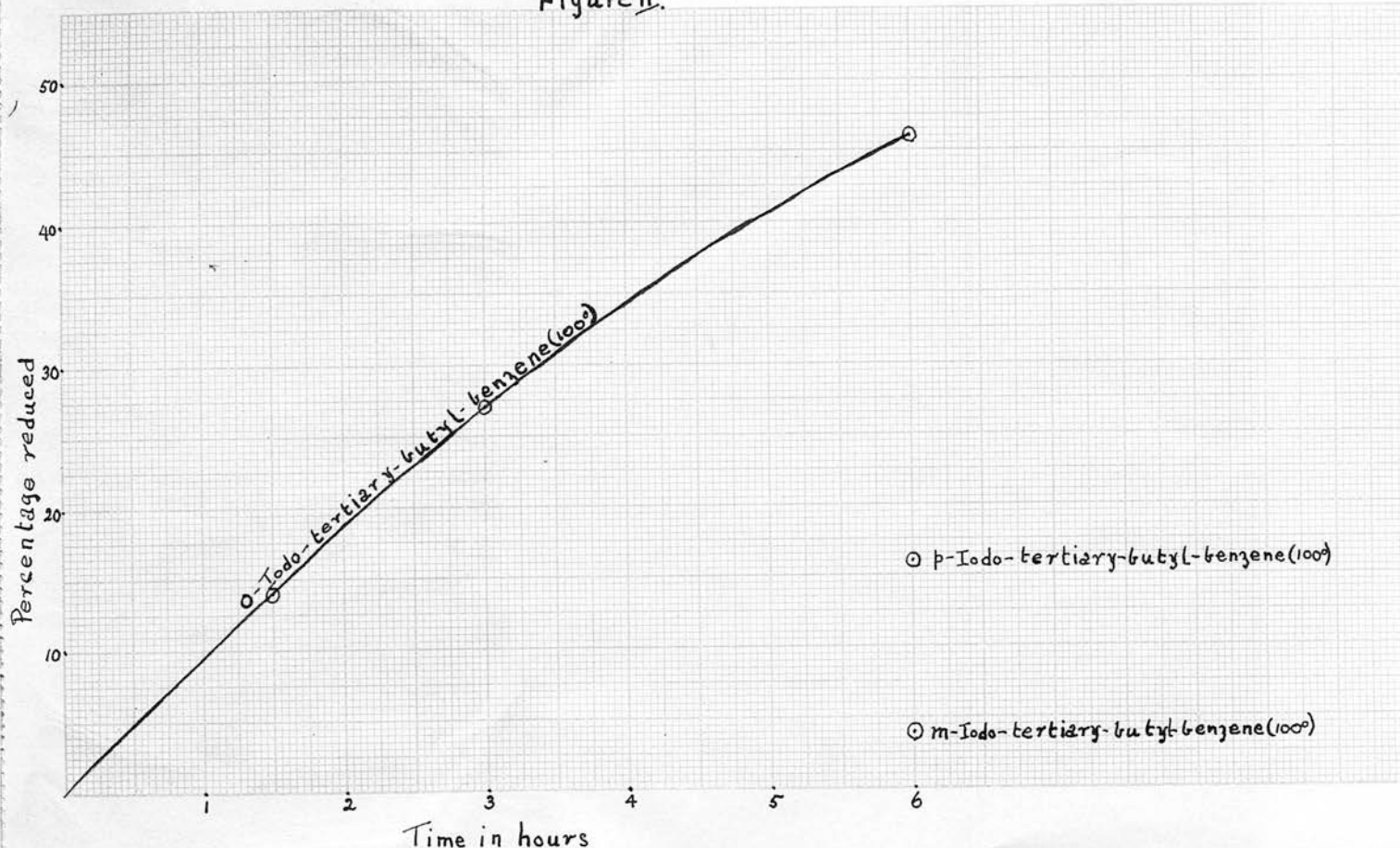


Figure II.



After a large number of fruitless attempts to obtain o-tertiary-butyl-benzyl bromide, it was decided to abandon the preparation. The meta- and para-isomerides were prepared with greater success and, in order to test the reactivity of the bromine atoms, were subjected to the action of (1) hydriodic acid and (2) aqueous alcohol.(compare p.3.).

It was found that with hydriodic acid in glacial acetic acid at 25°, there were indications that the meta-compound was slightly more reactive with liberation of iodine than was the para-isomeride.

From/

From the last experiment it was possible to isolate p-tertiary-butyl-benzyl iodide (identical with a sample prepared by a method which left no doubt as to its composition) after the bromide had stood in contact with the reagent for 4 days and again after 10 days. This point is also of importance, since it shows that no molecular rearrangement of the tertiary-butyl-group takes place in presence of hydriodic acid. At 100° and 110° , the order of ease of reduction was definitely meta > para. The results of these investigations are shown graphically in Figures III and IV.

Figure III.

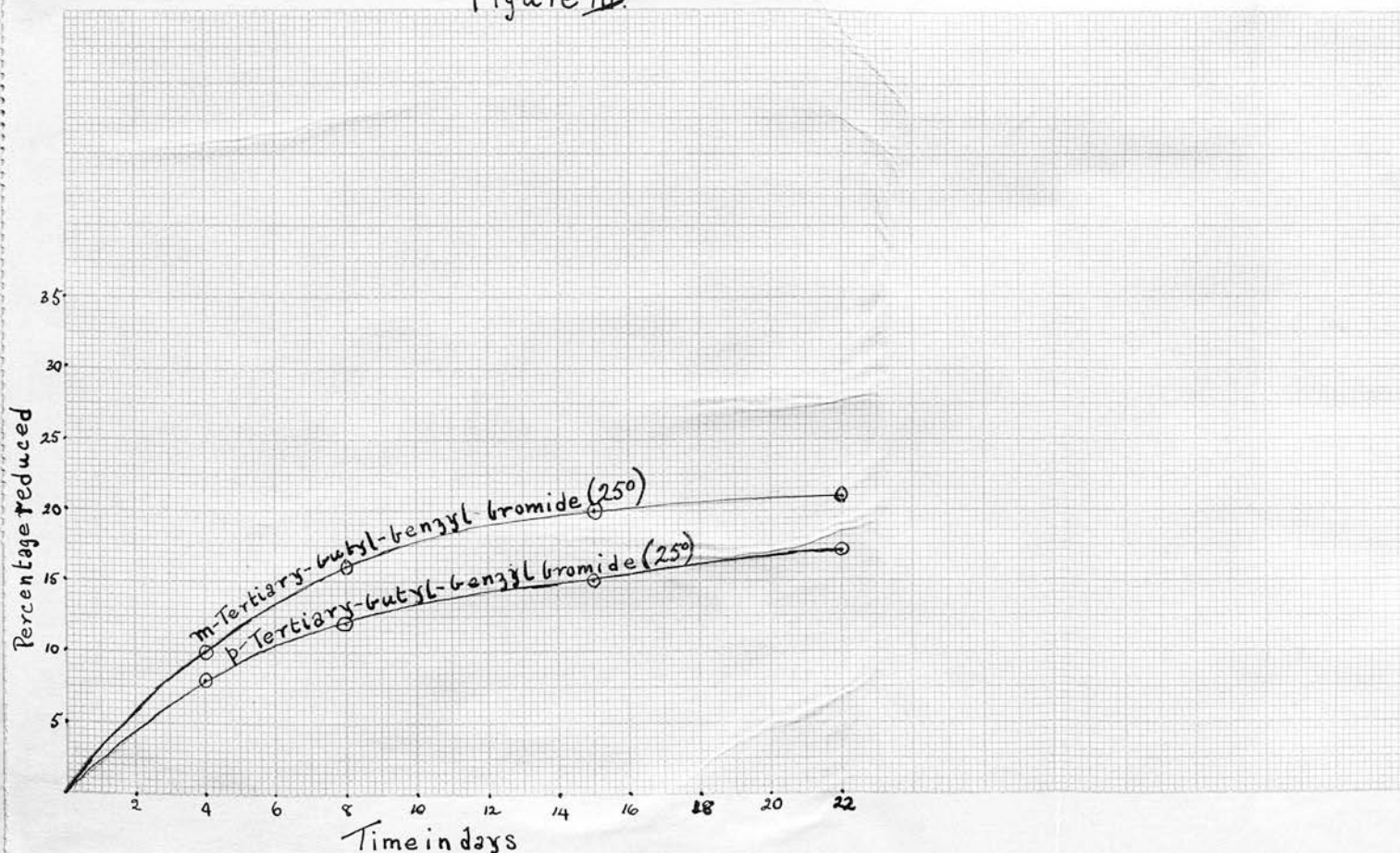
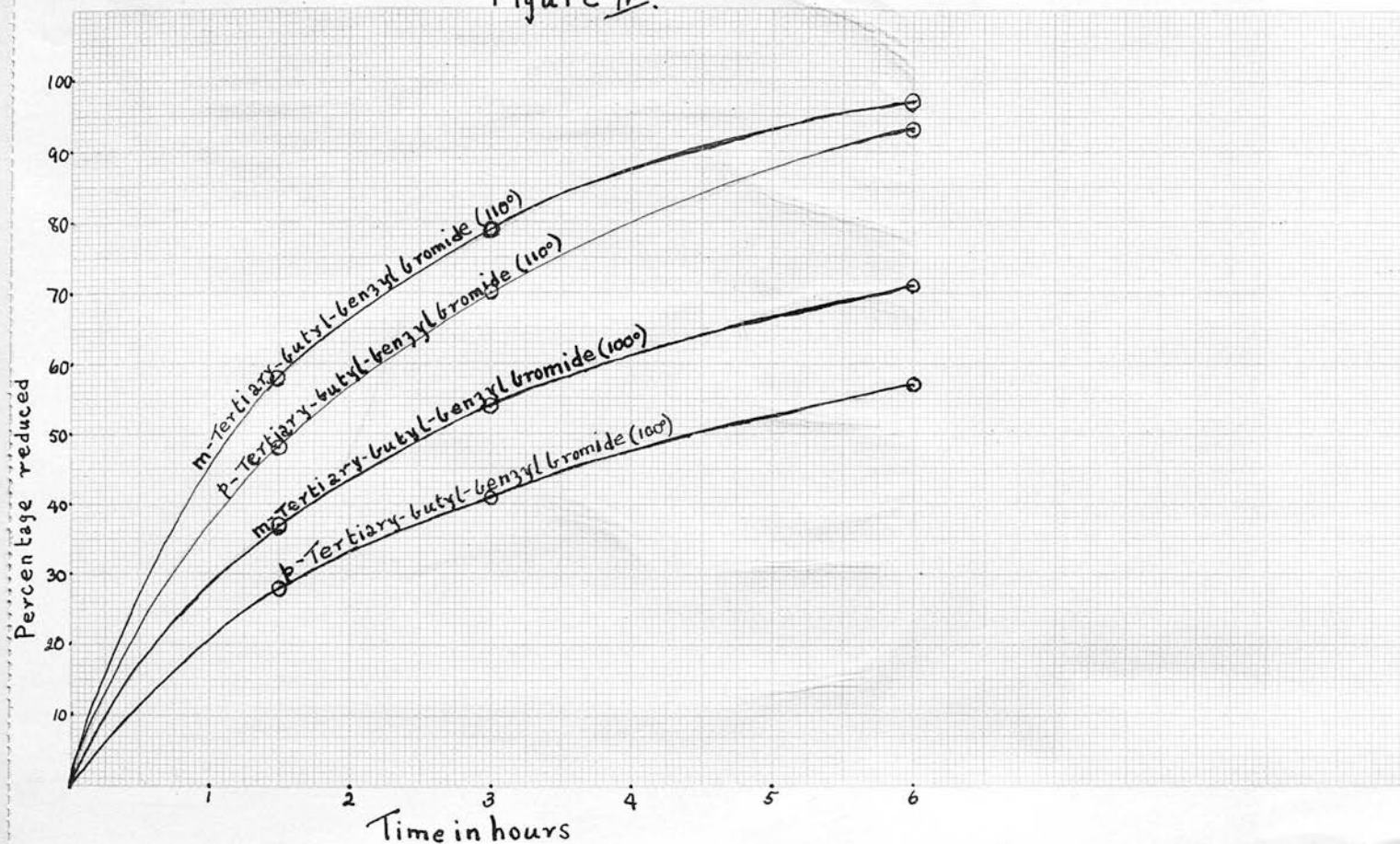


Figure IV.



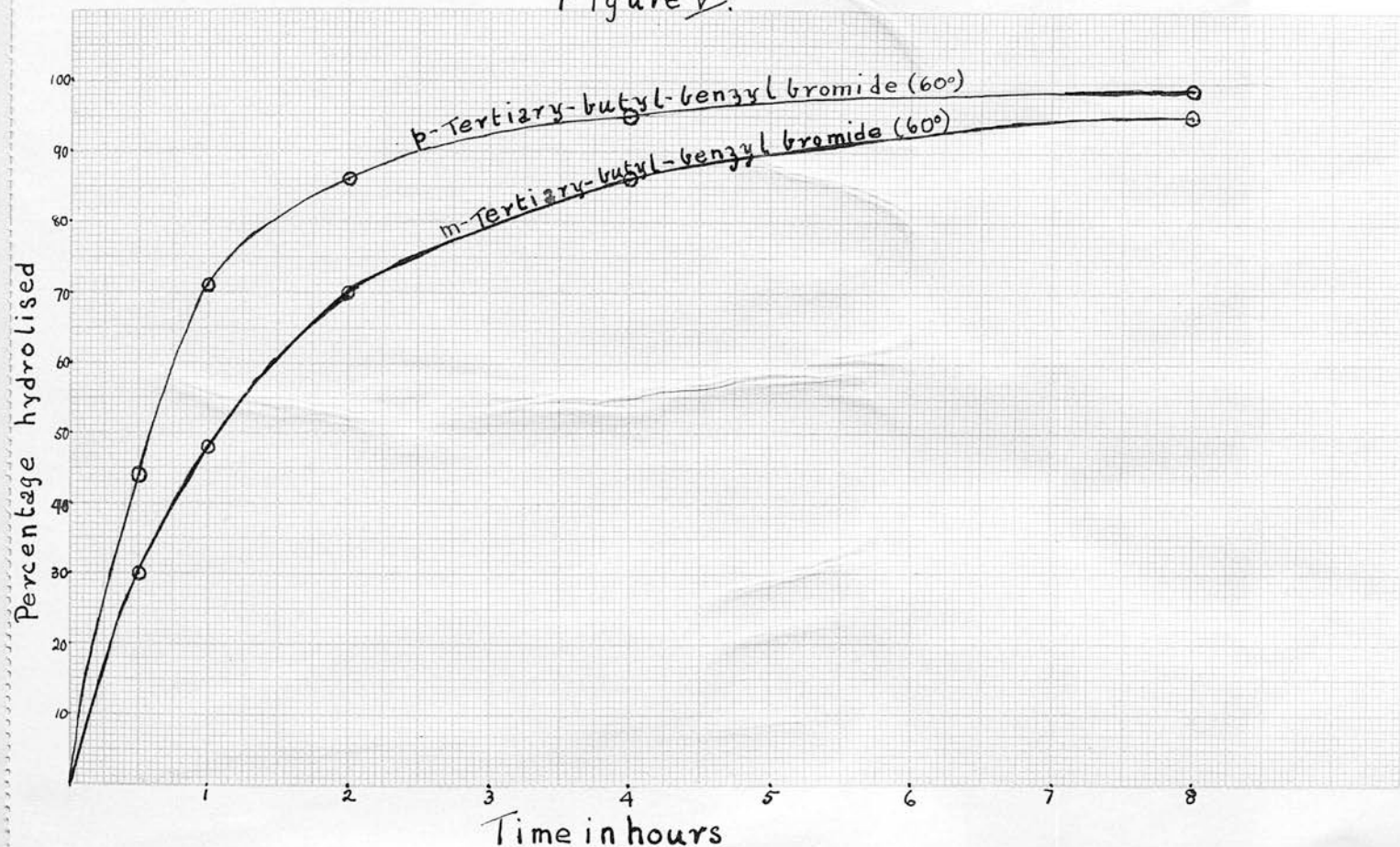
From the graphs in Figure IV it is possible to arrive at an approximate rate of reduction by determining the reciprocal of the time taken for 50 per cent of the compounds to undergo reaction (vide Shoesmith and Slater, J.C.S., 1926, 216). They are for the meta-isomeride, $K_{m_{100^\circ}} = 0.39$, $K_{m_{110^\circ}} = 0.87$, and for the para-isomeride, $K_{p_{100^\circ}} = 0.23$, $K_{p_{110^\circ}} = 0.63$. The values for unsubstituted benzyl bromide are $K_{u_{100^\circ}} = 0.20^*$, $K_{u_{110^\circ}} = 0.39^*$ and show that both compounds are more rapidly reduced than the unsubstituted benzyl bromide.

With/

*Shoesmith and Slater (loc.cit., p.217).

With aqueous alcohol the para-isomeride was more rapidly hydrolysed than the meta, as seen from Figure V.

Figure V.



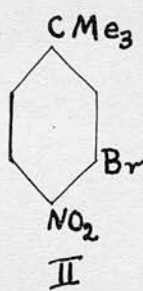
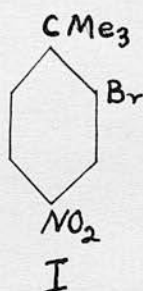
The approximate velocity constants at 60° have been determined as before and found to be $K_{m_{60}} = 0.95$ for the meta-compound, $K_{p_{60}} = 1.71$ for the para. At 25°, definite velocity constants were obtained and are

$k_{m_{25}} = 192 \times 10^{-6}$ for the meta-isomeride and $k_{p_{25}} = 333 \times 10^{-6}$ for the para. The values $K_{u_{60}} = 0.67$ (Shoosmith and Slater, loc. cit.) and $k_{u_{25}} = 125 \times 10^{-6}$ (Shoosmith and Rubli/

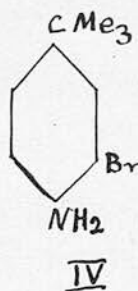
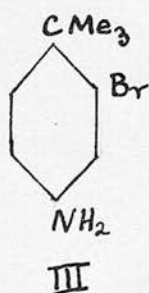
Rubli, J.C.S., 1927, 3099) show that the *m*- and *p*-tertiary-butyl-benzoyl bromides are more reactive than the unsubstituted compound. This proves that there is a definite transmission of an influence to the meta-position and that at this point, the reactivity is very definitely opposite from that in the para-position.

The dissociation constants of the isomeric tertiary-butyl-benzoic acids were determined at 25° and found to be $K_{o_{25^{\circ}}} = 2.8 \times 10^{-2}$, $K_{m_{25^{\circ}}} = 5.2 \times 10^{-3}$, $K_{p_{25^{\circ}}} = 4.2 \times 10^{-3}$ for the ortho-, meta- and para-isomerides respectively. The dissociation constant for benzoic acid is $K_{a_{25^{\circ}}} = 6.9 \times 10^{-3}$. Thus of the three acids, the ortho is stronger and the meta and para weaker than the unsubstituted benzoic acid.

In order to produce additional evidence that the ortho-position in tertiary-butyl-benzene is reactive, the following experiments were also carried out. After many unsuccessful attempts, using various catalysts, *p*-nitro-tertiary-butyl-benzene was slowly brominated in presence of very finely divided iron and a bromo-nitro-compound was obtained, which must have the constitution I or II:



On reduction, the corresponding amino-derivative was formed of constitution III or IV.



On acetylation of this, a compound, m.p. 142° - 143° , was produced. 3-Bromo-4-acetamino-tertiary-butylbenzene has m.p. 156° - 158° and when mixed with the acetamino-compounds obtained above, has m.p. 137° - 138° . Consequently the bromo-amino and bromo-nitro-derivatives have the constitutions represented by formulae III and I respectively, and the compound formed on elimination of the amino-group from III was o-bromo-tertiary-butylbenzene. This, taken in conjunction with the evidence obtained from the reduction of o-iodo-tertiary-butylbenzene, shows the activity of the ortho-position. It is noteworthy that the bromination of the p-nitro-derivative was very much slower than that of the corresponding toluene compound, a fact which is probably due to the large steric influence of the tertiary-butyl-group.

As may be seen from many foot notes, considerable confusion has arisen in the literature with respect to isobutyl- and tertiary-butyl-compounds.
Schramm/

Schramm (Monatsh., 1888, 9, 615) discovered that tertiary-butyl-benzene was formed by the action of isobutyl chloride on benzene in presence of aluminium chloride, and that the properties of the hydrocarbon obtained differed entirely from those of isobutyl-benzene prepared from bromobenzene and isobutyl bromide or iodide in presence of sodium. An "Umlagerung" has taken place, probably owing to the tendency of the symmetrical isobutyl-group to change into the symmetrical tertiary-butyl-group. This molecular rearrangement of the isobutyl- into the tertiary-butyl-group has also been observed by Baur (Ber., 1891, 24, 2832), who found that the hydrocarbon, obtained by the action of isobutyl chloride on toluene in presence of aluminium chloride, was identical with that obtained by employing tertiary-butyl-chloride instead of isobutyl chloride, that is, it was tertiary-butyl-toluene. Another interesting transformation, was observed by Verley (Bl., 1898, [3], 19 67), who obtained p-tertiary-butyl-toluene by the action of isobutyl alcohol on toluene in presence of sulphuric acid as condensing agent. The hydrocarbon can be oxidised to p-tertiary-butyl-benzoic acid, m.p. 164° , an acid, proved by Bialobrzewski (Ber., 1897, 30, 1773) not to be p-isobutyl-benzoic acid, as was formerly maintained, but the tertiary-butyl-compound in the following way.

By/

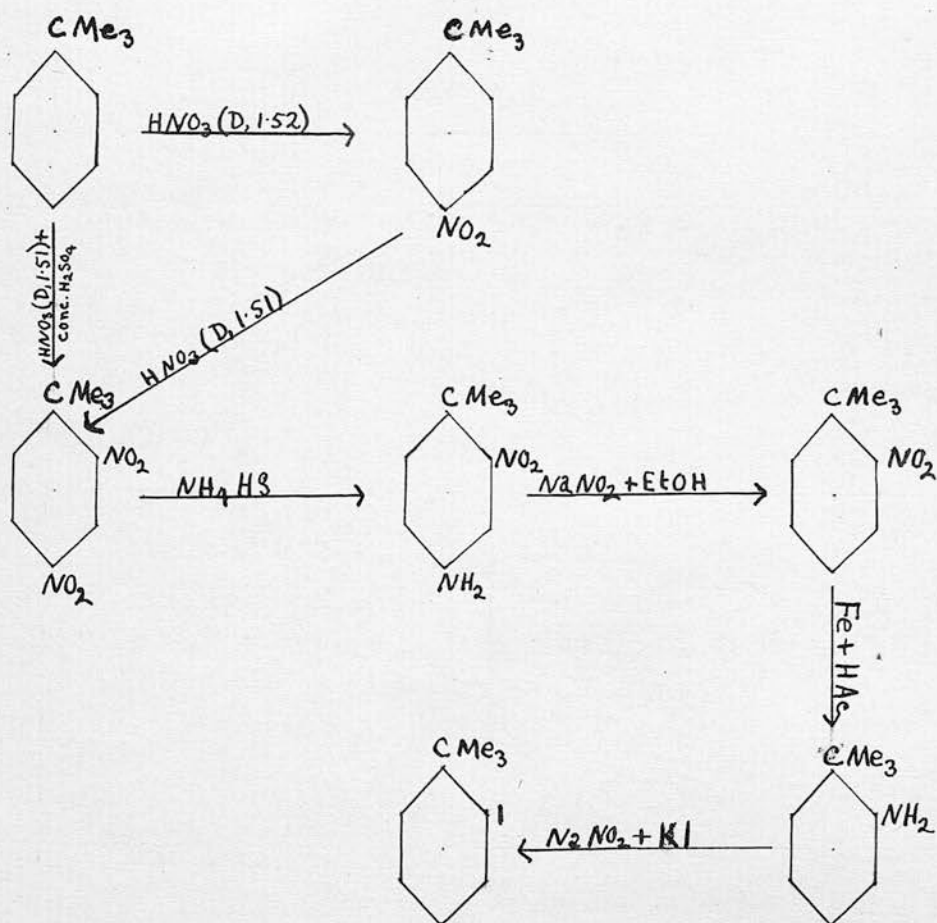
By the action of isobutyl chloride on toluene in presence of ferric chloride, Bialobrzewski obtained a hydrocarbon which was identical with that prepared when tertiary-butyl-chloride was used instead of isobutyl chloride, that is, the hydrocarbon was p-tertiary-butyl-toluene and the acid obtained on oxidation/^{p-}tertiary-butyl-benzoic acid.

This molecular rearrangement has probably caused ^{the}/perplexity, which has been remarked upon in the literature from time to time (vide Konowalow, Centr., 1899, I, 777; Willgerodt and Rampacher, Ber., 1901, 34, 3666; Anschütz and Rauff, Annalen, 1903, 327, 202, footnote; Beilstein, Handbuch der Organischen Chemie, Hamburg 1903, Vol. II, p. 845; Boedtker, Bl., 1906, [3], 35, 833; Reilly and Hickinbottom, J. C. S., 1920, 117, 105).

All the compounds described in this research are tertiary-butyl-benzene derivatives, since, (1) the iodo-tertiary-butyl-benzenes and o- and m-tertiary-butyl-benzoic acids were all prepared from tertiary-butyl-benzene, whilst (2) the m-tertiary-butyl-benzyl bromide used, gave m-tertiary-butyl-benzoic acid on oxidation (p. 48) and (3) p-tertiary-butyl-benzyl bromide was obtained from p-tertiary-butyl-toluene, which gave p-tertiary-butyl-benzoic acid identical with a specimen prepared from p-bromo-tertiary-butyl-benzene (p. 52).

PREPARATIVE.o-Iodo-tertiary-butyl-benzene.

o-Iodo-tertiary-butyl-benzene was obtained by means of the following series of reactions:

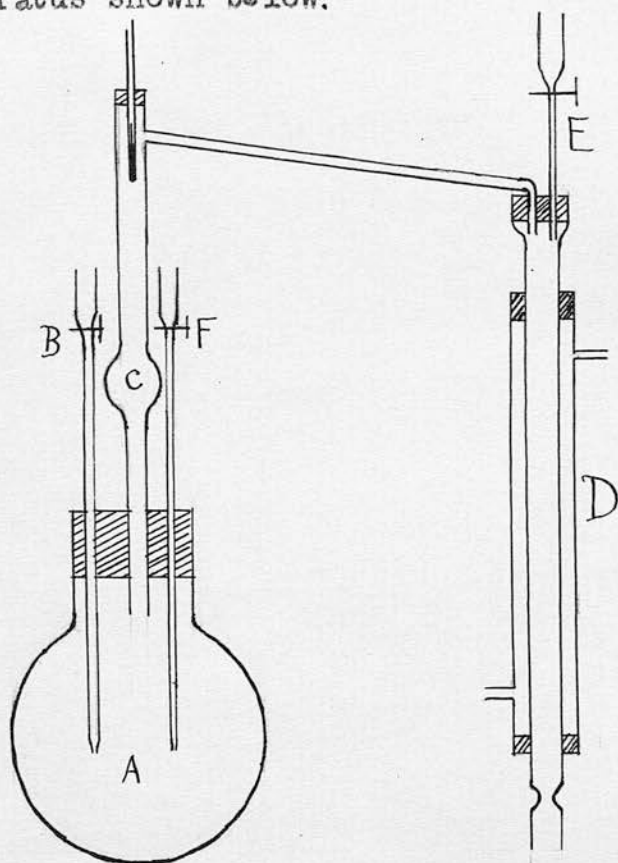
Tertiary-butyl-benzene.

prepared/

Tertiary-butyl-benzene was

prepared by the action of a mixture of iso- and tertiary-butyl-chlorides on benzene in presence of aluminium chloride.

The mixed butyl chlorides were obtained from isobutyl alcohol (b.p. 106.5° - 108.5°) by the method described by Dehn and Davies (J.A.C.S., 1907, 29, 1332) in the apparatus shown below.



Isobutyl alcohol (111 grams) was added as rapidly as the vigour of the reaction would permit from the dropping funnel B to phosphorus trichloride (102 grams) contained in the flask A, which was continually shaken and gently heated during the addition.

Hydrogen/

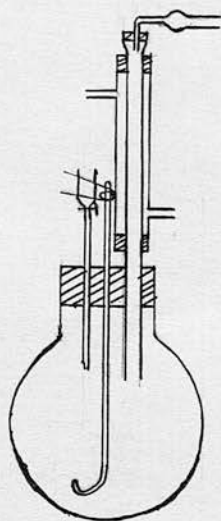
Hydrogen chloride was evolved and passed through the distillation column C to the condenser D which was filled with glass beads over which water dropped from E, in order to absorb the fumes. When all the alcohol had been added, a warm solution of 46 grams zinc chloride which boiled at 150° - 160° was admitted at intervals from the dropping funnel F in such a way that the zinc chloride dissolved immediately, a precaution which increases the yield considerably. During the zinc chloride addition, the reaction mixture was maintained at 70° and after the addition, the reaction product was completely distilled, the oil and water in the receiver separated, and the former washed in turn with water, sodium carbonate to remove acid and then again with water. The oil was dried over calcium chloride and fractionated, the portion boiling between 51° and 72° being collected separately, and was a mixture of iso- and tertiary-butyl chlorides. In this way 1217 grams of the chlorides were obtained from 3005 grams isobutyl alcohol, representing a yield of 32 per cent, which could not be improved (compare Dehn and Davis).

After taking all precautions as recommended by Dehn and Davis for avoiding the formation of secondary products, the reaction mixture was found to contain in addition to the chlorides, about 32 per cent of a higher boiling liquid which probably contains polymerides/

polymerides of isobutylene (Meyer and Jacobsen, Lehrbuch der Organischen Chemie, Berlin and Leipzig, 1922, Vol. I, part 1, p. 842).

The method by which normal butyl chloride is prepared (Norris, Organic Syntheses, New York, 1925, vol. V, p. 27), was found to be useless for the preparation of isobutyl chloride. Isobutyl alcogol along with a solution of anhydrous zinc chloride in concentrated hydrochloric acid were heated under a reflux condenser for approximately 4 hours, the reaction mixture was allowed to cool and the upper layer separated from the zinc chloride and reheated for half an hour with an equal volume of concentrated sulphuric acid in the same way. The reaction product was then distilled, the distillate washed with water and dried over calcium chloride, but no isobutyl chloride could be detected, even when the reaction was carried out under other conditions.

Tertiary butyl benzene was prepared by the method described by Schramm (Monatsh., 1888, 9, 615) in the apparatus shown below.



Finely powdered anhydrous aluminium chloride (one part by weight) was mixed with benzene (3 parts) and the mixture cooled in ice. The flask was fitted with a three holed cork, carrying (a) a condenser, in turn closed by a calcium chloride tube, (b) a dropping funnel and (c) a stirrer, since it was found that the yield was greatly increased when the reaction mixture was stirred. The mixture of chlorides (one part) was added slowly in small quantities at intervals, hydrogen chloride being evolved. After the addition of the chlorides, the action was allowed to proceed for about 48 hours. (To ensure success in this preparation, all reagents and apparatus must be dry and the reaction mixture maintained approximately at 0° , since the yield of tertiary-butyl-benzene decreases if the temperature is allowed to rise). The product was then poured in portions into a flask containing ice, the benzene layer separated, washed with aqueous sodium hydroxide and heated with the same reagent for approximately half an hour by means of a moderately rapid current of steam passed into the mixture. After separation, the benzene layer was washed in turn with dilute hydrochloric acid, water, and finally dried over calcium chloride, after which it was fractionated, when the benzene was collected separately. The whole of the distillate except the benzene was refractionated over sodium until the tertiary-butyl-benzene had a b.p. between 164° and 170° . It was found that if the tertiary/

tertiary-butyl-benzene were fractionated over sodium immediately after the benzene had been removed, the yields were considerably decreased. From 1620 grams iso- and tertiary-butyl chlorides, including 450 grams tertiary-butyl chloride (Kahlbaum), 624.5 grams tertiary-butyl-benzene were obtained, representing a yield of 27 per cent.

Note on the preparation.

The course of the reaction depends to a large extent on the quality of the aluminium chloride employed and much more satisfactory yields were obtained when white anhydrous aluminium chloride was used.

Anhydrous aluminium chloride is usually yellow owing to the presence of chlorides of iron, sulphur, etc., (vide Watts' Dictionary of Chemistry, London, 1888, vol. I, p. 144), and it appears as if the chlorides of iron act ^{as} additional catalysts in the Friedel-Craft reaction causing the formation of further substituted derivatives, thus explaining the poor yields obtained in some of the experiments. The white aluminium chloride gave much clearer distillation residues which crystallised out on cooling as a white solid. This readily crystallised from hot alcohol in plates, m.p. 124° - 125°, and is impure tri-tertiary-butyl-benzene which is probably the 1:2:3-derivative, m.p. 128°. Di-tertiary-butyl-benzene melts at 70°. Senkowski (Ber., 1890, 23, 2420), compare Schramm (loc. cit.).

When/

When the reaction mixture from experiments in which white aluminium chloride had been used was poured on to ice, there was formed a red solid, which separated from the benzene layer containing the bulk of the tertiary-butyl-benzene. This red solid on the addition of water gave more tertiary-butyl-benzene. On the other hand when yellow aluminium chloride was used, a red oil was formed, from which little tertiary-butyl-benzene could be isolated.

Verley's method (Bl., 1898. [3] 19,72)* for the preparation of tertiary-butyl-benzene was also investigated. Fuming sulphuric acid (4 parts by weight) was added slowly during three quarters of an hour to a mixture of iso-butyl alcohol (one part) and benzene (4 parts), the reaction flask being cooled and shaken. The reaction mixture was washed with water, and the upper layer separated and distilled, dried over calcium chloride and fractionated. The yield of tertiary-butyl-benzene was poor and when the reaction was carried out later at 50° and 80°, a large quantity of higher boiling liquid was formed.

* Verley described ^{the} tertiary-butyl-benzene as isobutylbenzene.

p-Nitro-tertiary-butyl-benzene.

p-Nitro-tertiary-butyl-benzene was prepared from tertiary-butyl-benzene by the method described by Malherbe (Ber., 1919, 52, 320). Concentrated nitric acid (D, 1.52) was added gradually to an equal weight of the hydrocarbon, the mixture being stirred for 2 hours at ordinary temperatures (compare Malherbe). Water was added, when a yellow oil separated, which was washed with water, dried over calcium chloride and fractionated under diminished pressure, using a modification of the Widmer flask. (Helv. Chim. Acta, 1924, 7, 59). From 351 grams tertiary-butyl-benzene (including 60 grams from an outside source) 233.5 grams p-nitro-tertiary-butyl-benzene, distilling at 124.5° – 129.5° /10 mm, were obtained, representing a yield of 50 per cent.

Seńkowski (loc.cit., p. 2414) obtained p-nitro-tertiary-butyl-benzene by the nitration of tertiary-butyl-benzene and describes the compound as a solid of m.p. 30° . Malherbe (loc.cit. p. 319) obtained this compound as a liquid, b.p. 265 – 267° /757 mm.

Seńkowski actually separated the para-isomeride from a nitration mixture, which contained ortho- and para-compounds, and it may have been therefore absolutely free from ortho-compound. It was never found possible to repeat his observation. Baur (Ber, 1894, 27, 1610) obtained an oil by the nitration of tertiary-butyl-benzene. He did not state what its composition was, but it was ^{probably} chiefly p-nitro-tertiary-butyl-benzene.

2:4-Dinitro-tertiary-butyl-benzene.

Malherbe's method (~~Baur~~, loc.cit., p.321) was used for the preparation of this compound. A mixture of nitric acid (2 parts by weight, D.1.51) and concentrated sulphuric acid (3 parts) was added during the course of 5 hours to tertiary-butyl-benzene (one part) maintained at a temperature of 60° , the contents of the reaction flask being constantly stirred during the nitration. The product was poured on to ice when a yellow oil separated, which solidified on standing. (N.B. Malherbe's product only solidified after the oil had been subjected to a vacuum distillation). The solid was filtered, washed with water and recrystallised from aqueous alcohol from which the dinitro-compound was obtained as a white crystalline solid becoming bright yellow on exposure to light. Both Malherbe and Baur describe it as a yellow crystalline solid. From 300.5 grams tertiary-butyl-benzene, 269.5 grams dinitro-tertiary-butyl-benzene were obtained, representing a yield of 54 per cent. It had m.p. 61° - 62° [Malherbe gives 61° - 62° , Baur(loc.cit.) 61° - 62°].

The dinitro-compound was also obtained from p-nitro-tertiary-butyl-benzene, prepared as above, by heating the well stirred p-nitro-compound at 60° for 2 to 4 hours (depending on the quality of the p-nitro-derivative) with an equal weight of nitric acid (D.1.51).

2-Nitro-4-amino-tertiary-butyl-benzene.

Finely divided 2:4-dinitro-tertiary-butyl-benzene (20 grams) was added to a mixture of ethyl alcohol (76 c.c.) and ammonia (D,0.880, 10 c.c.) and hydrogen sulphide passed into the mixture for one hour; the reaction flask was occasionally agitated. The mixture was then heated on the steam bath for a few minutes, cooled, and the process repeated. To the reaction mixture an excess of water was added, when the nitro-amino-compound, precipitated as a yellow solid and mixed with sulphur, formed during the reduction, was filtered, washed with water and heated under a reflux condenser with an excess of hydrochloric acid (D,1.05) for 5 minutes. The solution was filtered from sulphur, the filtrate cooled until hydrochloride commenced to crystallise out, when an excess of ammonia (D,0.880) was immediately added. The nitro-amine separated as an oil, which rapidly solidified, and was filtered off, washed with water and pressed on a porous tile. The small amount of tar formed during the reduction was eliminated by efficient treatment on the porous tile. In this way 185.5 grams 2-nitro-4-amino-tertiary-butyl-benzene were obtained from 302.5 grams dinitro-tertiary-butyl-benzene, representing a yield of 71 per cent. 2-nitro-4-amino-tertiary-butyl-benzene crystallises from aqueous alcohol as plates, from petrol ether as needles of m.p. 54.5° - 55.5° . Found: N, 14.7 $C_{10}H_{14}O_2N_2$ requires N, 14.4 per cent. It/

It gives a hydrochloride, m.p. 209.5° - 210.5° .

2-Nitro-4-acetamino-tertiary-butyl-benzene was prepared by gently boiling the corresponding amine-compound with acetic anhydride for 5 minutes. The acetamino-derivative was precipitated by adding water when cold, filtered and washed with water. It crystallised from aqueous alcohol in colourless needles m.p. 110° - 112° .

o-Nitro-tertiary-butyl-benzene.

It was not found possible to prepare o-nitro-tertiary-butyl-benzene by direct nitration of the hydrocarbon,* although Senkowski (loc.cit.) was successful in separating both the ortho- and the para-derivatives from a nitration mixture of the two isomerides, the former being an oil, b.p. 247.4° - 248.4° / 737.8 mm.

o-Nitro-tertiary-butyl-benzene was satisfactorily obtained by elimination of the amino-group from 2-nitro-4-amino-tertiary-butyl-benzene. 2-nitro-4-amino-tertiary-butyl benzene (one part by weight) was diazotised in presence of absolute alcohol (3 parts) and concentrated sulphuric acid (3 parts). After addition of the sulphuric acid to the alcoholic solution of the nitroamine, the mixture was cooled to 0° , when the sulphate crystallised out. An excess of a saturated solution of sodium nitrite was slowly added, the reaction mixture being vigorously stirred, and/

* o-Nitro-tertiary-butyl-benzene could not be obtained by nitration of p-aminotertiary-butyl-benzene (vide p. 35) in presence of sulphuric acid and subsequent elimination of the amino-group. (compare Reilly and Hickinbottom, J.C.S., 1920, 117, 115).

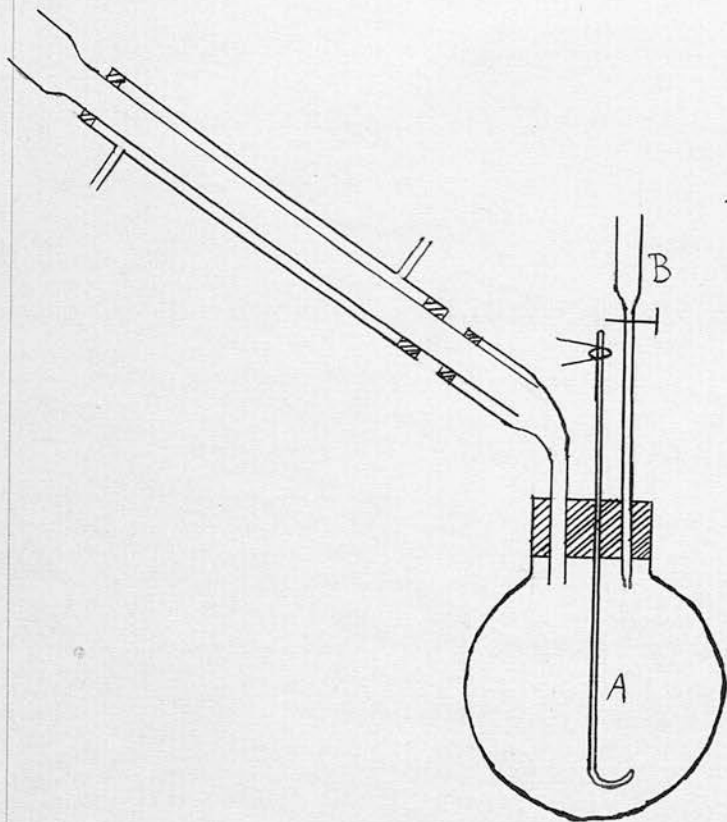
and the temperature maintained approximately at 0° . The diazo-compound was decomposed on the steam bath, and the product steam distilled. The nitro-compound was extracted from the distillate with ether, and the ethereal extract washed in turn with aqueous sodium hydroxide, water, and dried over sodium sulphate. After distilling off the ether, the o-nitro-tertiary-butyl-benzene was distilled under reduced pressure, when the liquid distilling at $113^{\circ}/10$ mm. - $115^{\circ}/10$ mm. was collected. It had b.p. $250.5^{\circ}/765$ mm. Eighty grams o-nitro-tertiary-butyl-benzene were obtained from 162.5 grams 2-nitro-4-amino-tertiary-butyl-benzene, representing a yield of 54 per cent. The nitro-compound is a yellow, peculiarly smelling oil.

Attempts were made to oxidise the oil to o-nitro-benzoic acid, using nitric acid of various strengths, with unsuccessful results. The difficulty of oxidation of such compounds has been remarked upon by Senkowski (loc.cit.) and also Malherbe (loc.cit.) and only the latter was successful in oxidising the p-nitro-compound to p-nitro-benzoic acid (compare introduction p. 7).

o-Amino-tertiary-butyl-benzene/

o-Amino-tertiary-butyl-benzene.

o-Nitro-tertiary-butyl-benzene was reduced to the corresponding amino-derivative by means of iron filings and glacial acetic acid in the apparatus shown below.



Fine iron filings (12 grams) were mixed with

15 c.c./

15 c.c. water and the mixture slowly stirred in the flask A, which was gently heated, whilst 1 c.c. glacial acetic acid and 0.3 c.c. o-nitro-tertiary-butyl-benzene were added from the dropping funnel B. The contents of the flask were heated to 90° , and at this temperature 10 grams o-nitro-compound were slowly added from B, an operation which occupied approximately 3 hours. The reaction mixture was well stirred during and after the addition, and the reaction was completed in approximately 2 hours, when no odour of nitro-compound was perceptible. The amine, so obtained, was steam distilled, extracted with ether, dissolved in dilute hydrochloric acid and unchanged nitro-compound extracted twice with ether. The amine was precipitated from the hydrochloric acid solution on addition of an excess of ammonia (D.O.880) and extracted with ether. The ethereal solution was washed with water, dried over sodium sulphate and after evaporation away of the ether, the amine was distilled under reduced pressure, and had b.p. $102^{\circ}/10$ mm. Fifty grams were obtained from 80 grams of o-nitro-tertiary-butyl-benzene, representing a yield of 75 per cent. The amine is a colourless liquid, very volatile in steam, becoming red on exposure to air, when a small quantity of colourless crystals, probably carbonate, separated: (compare Senkowski loc. cit.^{p. 2415}). Refractive Index 1.5451 at 16.5° for ordinary light.

o-Acetamino/

o-Acetamino-tertiary-butyl-benzene was prepared in the same way as the 2-nitro-4-acetamino-derivative. It recrystallised from benzene in prismatic needles and had m.p. 161° - 162° Senkowski (ibid, 2416) gives 159° .

o-Iodo-tertiary-butyl-benzene.

Dilute sulphuric acid (60 c.c., D, 1.12) was added to o-amino-tertiary-butyl-benzene (5.5 grams). This was well stirred during the addition to ensure the formation of a finely divided precipitate of the amine sulphate, to facilitate diazotisation, which was effected by means of a solution of 5 grams sodium nitrite in 10 c.c. water. After this operation a solution containing 15 grams potassium iodide in 25 c.c. water was added. This was a difficult experiment to bring to a successful conclusion, and it was found, that during the additions of sodium nitrite and potassium iodide, very vigorous stirring was essential, whilst the mixture was cooled to -10° , at which temperature, it was found necessary to carry out the operation, as the diazonium sulphate is very unstable and begins to decompose at about -8° *. It was also found advantageous to add the potassium iodide rapidly. The amine and diazonium sulphates are very insoluble, a fact which rendered diazotisation extremely difficult. After the addition of potassium iodide, the reaction mixture was allowed to reach ordinary temperatures, and after an/

* This instability of the diazonium compound is paralleled in the corresponding toluene derivative, since o-tolyl-diazonium chloride is a very unstable compound, as compared with its para-isomeride.

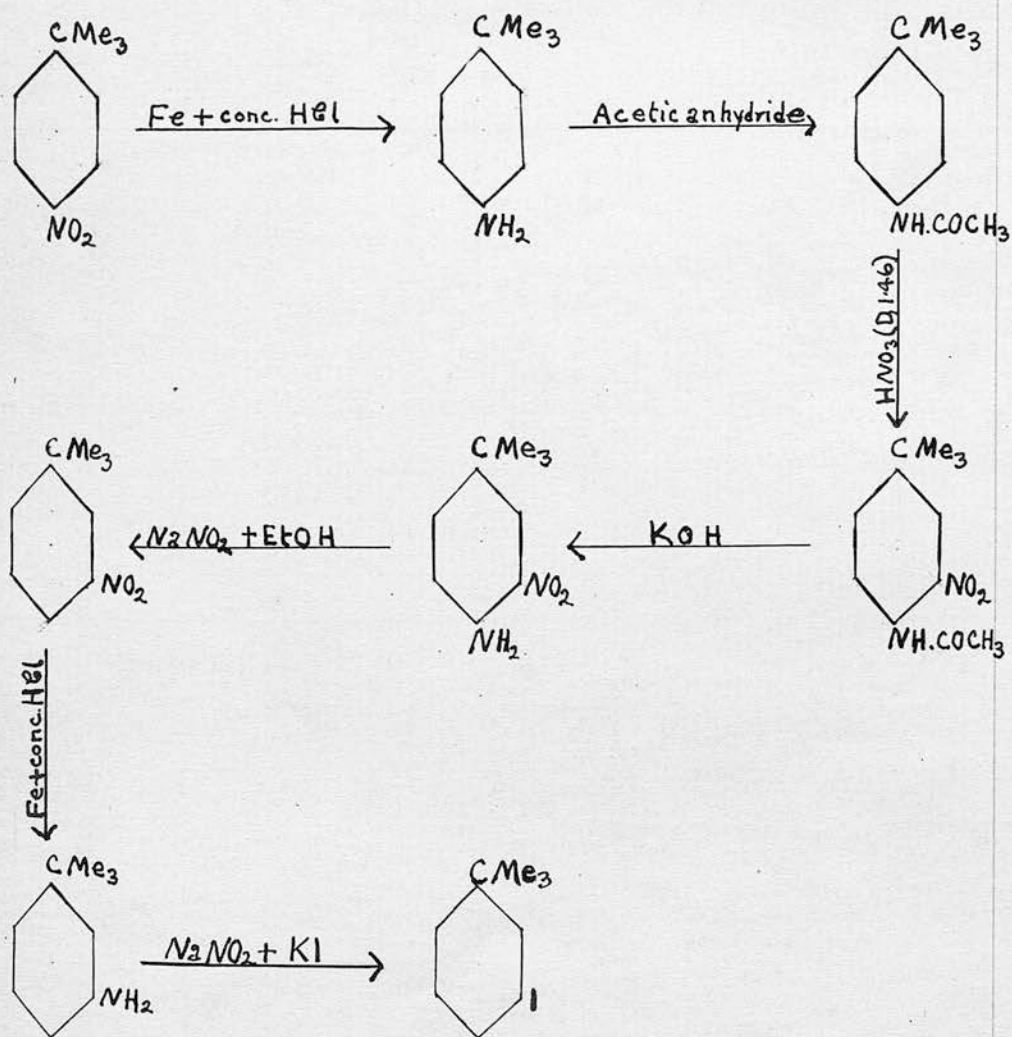
an hour, when the diazonium iodide had almost completely decomposed, decomposition was completed by heating on the steam bath. A dark coloured oil separated. To this alkali was added to remove free iodine and the compound distilled over in steam. The distillate was extracted with ether, and the ethereal solution washed in turn with (a) aqueous sodium hydroxide to remove phenol, (b) water, (c) dilute hydrochloric acid to remove unchanged base, (d) again with water, and finally dried over sodium sulphate. After evaporation away of the ether, the iodo-compound was distilled in vacuo, using a modification of the Widmer flask. It had b.p. $115^{\circ}/10 \text{ mm.} - 118^{\circ}/10 \text{ mm.}$ Found: I, 48.3 $\text{C}_{10}\text{H}_{13}\text{I}$ requires I, 48.8 per cent. In this way 9 grams o-iodo-tertiary-butyl-benzene were obtained from 39 grams o-amino-tertiary-butyl-benzene, representing a yield of 13 per cent. In addition, a liquid (2.5 grams), which distilled at $99^{\circ}/10 \text{ mm} - 103^{\circ}/10 \text{ mm.}$ and contained 20.6 per cent of iodine (obviously the iodo-compound was present), was also obtained. Immediately before the addition of potassium iodide, a dark coloured plastic substance was rapidly formed. It was found, that on one occasion, when the formation of this product did not occur, no low-boiling-point fraction was obtained. This substance did not appear to contain tertiary-butyl-benzene, but was insufficient for further investigation, and hence no conclusion could be arrived at, as to the cause of its appearance.

When/

When diazotisation was performed in more dilute solution, the diazonium sulphate was slightly more stable, but diazotisation was not so satisfactory. The yield of the iodo-compound was not increased, when the temperature was allowed to rise after diazotisation and excess nitrous acid removed from the mixture, with urea.

m-Iodo-tertiary-butyl-benzene.

m-Iodo-tertiary-butyl-benzene was obtained by means of the following series of reactions:



p-Amino-tertiary-butyl-benzene.

p-Amino-tertiary-butyl-benzene was obtained by reduction of the p-nitro-compound with iron and concentrated hydrochloric acid. The method was similar to that described for the preparation of the ortho-isomeride. After steam distillation, the amine was extracted with ether and the ethereal solution dried over sodium sulphate. After evaporation away of the ether, the amine was distilled, when it had b.p. 238° (Malherbe, loc.cit., p.322 gives 238° - 240°). In this way 106 grams p-amino-tertiary-butyl-benzene were obtained from 169 grams p-nitro-tertiary-butyl-benzene, representing a yield of 75 per cent. The amine was acetylated (vide below), the acetamino-compound purified by recrystallisation from alcohol, hydrolysed, and thus the amine was obtained quite pure.

p-Acetamino-tertiary-butyl-benzene.

The heating of p-amino-tertiary-butyl-benzene under a reflux condenser with glacial acetic acid and a small quantity of anhydrous zinc chloride for two hours was found to be unsatisfactory for the preparation of its acetyl-derivative.

The method indicated by Malherbe (loc.cit.) was employed. Excess acetic anhydride was added to p-amino-tertiary-butyl-benzene, when the acetyl-derivative was readily formed as a crystalline mass, which/

which was filtered, washed with acetic anhydride, pressed on a porous tile and recrystallised from alcohol. It had m.p. 169° [Malherbe gives 169° - 170° ; s \acute{e} nkowski (loc.cit., p. 2417) 172°]. In this way 92 grams p-acetamino-tertiary-butyl-benzene were obtained from 106 grams p-amino-tertiary-butyl-benzene, representing a yield of 68 per cent.

3-Nitro-4-acetamino-tertiary-butyl-benzene.

p-Acetamino-tertiary-butyl-benzene (one part by weight) was carefully added to a well stirred mixture of nitric acid (D., 1.52, 2 parts) and nitric acid (D., 1.40; 2 parts). The temperature was allowed to rise to, and maintained at 35° - 40° . The product was allowed to stand for a short time and then poured into a large excess of water, when the 3-nitro-4-acetamino-compound was precipitated. The precipitate was filtered, washed with water and dried on a porous tile.

? Yield
m.p.

The method was unsatisfactory when nitric acid (4 parts; D., 1.52) was used, owing to tarring.

3-Nitro-4-amino-tertiary-butyl-benzene.

A saturated aqueous solution of 17 grams potassium hydroxide was added to a hot saturated alcoholic solution of 36 grams 3-nitro-4-acetamino-tertiary-butyl-benzene. Heat was evolved and the reaction was completed by boiling until the odour of ammonia was perceptible. The dark red liquid obtained was poured into a large excess of water, when the brown/

brown-yellow precipitate formed, was filtered, washed with water and dried on a porous tile. Twenty-four grams 3-nitro-4-amino-tertiary-butyl-benzene were obtained, representing a yield of 81 per cent.

m-Nitro-tertiary-butyl-benzene.

m-Nitro-tertiary-butyl-benzene was obtained from 3-nitro-4-amino-tertiary-butyl-benzene by elimination of the amino-group, as described in the preparation of o-nitro-tertiary-butyl-benzene. The m-nitro-derivative distilled at 93° - 122° /9 mm. The liquid was obviously impure, but it was found that on reduction, a pure sample of the amine could be obtained. 12 grams m-nitro-tertiary-butyl-benzene were obtained from 24 grams 3-nitro-4-amino-tertiary-butyl-benzene.

m-Amino-tertiary-butyl-benzene.

m-Amino-tertiary-butyl-benzene was obtained from m-nitro-tertiary-butyl-benzene which was reduced by iron filings and a small quantity of concentrated hydrochloric acid, as described in the preparation of the p-amino-derivative. Six grams m-amino-tertiary-butyl-benzene, distilling at 107° - 108° /9 mm., were obtained from 12 grams m-nitro-tertiary-butyl-benzene. The amine was purified by acetylation and hydrolysis of the acetamino-compound so obtained. Acetylation was effected in a way similar to that by which the 2-nitro-4-acetamino-derivative was prepared.

m- /

m-Acetamino-tertiary-butyl-benzene was recrystallised from aqueous alcohol, when it had m.p. 97° - 99° .

[Gelzer* (Ber., 1888, 21, 2949) gives 101°]. Four grams of the m-acetamino-derivative were obtained from 6 grams of the corresponding amine.

The m-acetamino-compound was hydrolysed by heating with a mixture of equal volumes (4 c.c.) of ethyl alcohol and concentrated hydrochloric acid for 3 hours. The pure amine (2 grams) was obtained from its hydrochloride so formed, by the addition of an excess of aqueous sodium hydroxide.

m-Iodo-tertiary-butyl-benzene.

m-Iodo-tertiary-butyl-benzene was obtained from the m-amino-derivative by a method, similar to that by which the ortho-derivative was prepared. During the gradual addition of sodium nitrite followed by potassium iodide, the temperature was maintained only below 10° and vigorous stirring was not essential (compare the preparation of the ortho isomeride). One and a half grams of m-iodo-compound were obtained from 2 grams m-amino-tertiary-butyl-benzene, representing a yield of 43 per cent.

m-Iodo-tertiary-butyl-benzene is a reddish-coloured liquid. It had b.p. 106° - 108° / 9 mm.

Found: I, 48.4. $C_{10}H_{13}I$ requires I, 48.8 per cent.

*This compound is described by Gelzer as an isobutyl-benzene derivative, but is in reality m-acetamino-tertiary-butyl-benzene.

p-Iodo-tertiary-butyl-benzene.

p-Acetamino-tertiary-butyl-benzene (20 grams) was hydrolysed in the same way as was the corresponding meta-compound. Eleven grams of pure amine were thus obtained.

p-Iodo-tertiary-butyl-benzene was obtained from the amine by the method employed in the preparation of the meta-isomeride. The iodo-compound distilled at 115.5° – $117.5^{\circ}/9$ mm. (compare Willgerodt and Rampacher, Ber., 1901, 34, 3669; Pahl, Ber., 1884, 17, 1233*; Boedtker, Bl., 1906, [3], 35, 832). Seven grams p-iodo-tertiary-butyl-benzene were obtained, representing a yield of 37 per cent.

m-Tertiary-butyl-benzyl-bromide.

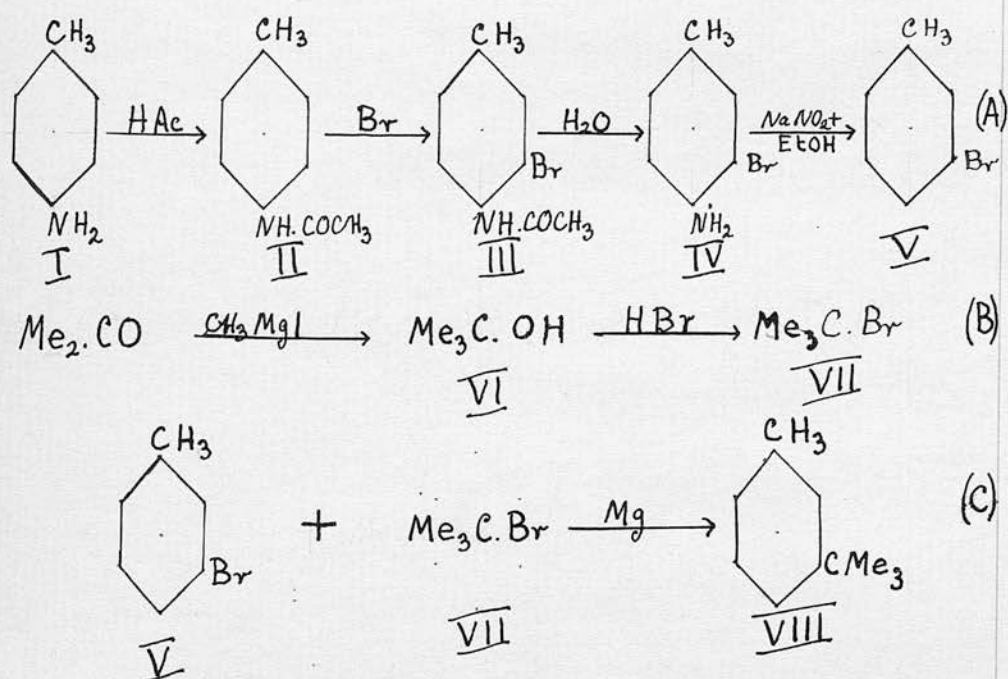
m-Tertiary-butyl-benzyl-bromide was prepared by the bromination of m-tertiary-butyl-toluene, in turn obtained by the method outlined by Baur (Ber., 1891, 24, 2832), in a manner, similar to that by which tertiary-butyl-benzene was prepared from iso- and tertiary-butyl-chlorides, the temperature of the reaction being somewhat higher than in the latter case. The same quantities of the reagents were employed; toluene being substituted for benzene. The yield of m-tertiary-butyl-toluene was poor.

It is remarkable, that in the reaction, the methyl-group directs the entering tertiary-butyl-group into/

* Pahl describes the iodo-compound as a derivative of isobutyl-benzene.

into the meta-position, since when sulphuric acid was used as condensing agent, the tertiary-butyl-group entered the para-position. By oxidising the butyl-toluene with chromic acid, Baur obtained isophthalic acid, which proved that the hydrocarbon belonged to the meta-series.

An attempt was therefore made to prepare the compound by reactions summarised as follows:



3-Bromo-4-amino-toluene (IV) was prepared by the method given in Organic Syntheses, New York 1926, vol. VI, p. 8. p-Toluidine (I) was converted into its acetamido-derivative (II), which with an excess of bromine gave 3-bromo-4-acetamino-toluene (III), and this on hydrolysis yielded 3-bromo-4-amino-toluene (IV). m-Bromotoluene/

m-Bromo-toluene (V) was obtained by the elimination of the amino-group from IV by diazotisation in presence of concentrated sulphuric acid and alcohol, and decomposition of the resulting diazo-compound with copper powder. The product was steam distilled and the oil obtained separated when it was washed in turn with aqueous sodium hydroxide, water, concentrated sulphuric acid and sodium carbonate, dried over calcium chloride and fractionated. (Bigelow, Johnson and Sandborn, Organic Syntheses, New York 1926, vol. VI, p. 16).

Tertiary-butyl-alcohol (VI) was prepared by the action of acetone on magnesium methyl¹iodide. (Vanino, Präparative Chemie, Stuttgart 1923, vol. II, p. 36).

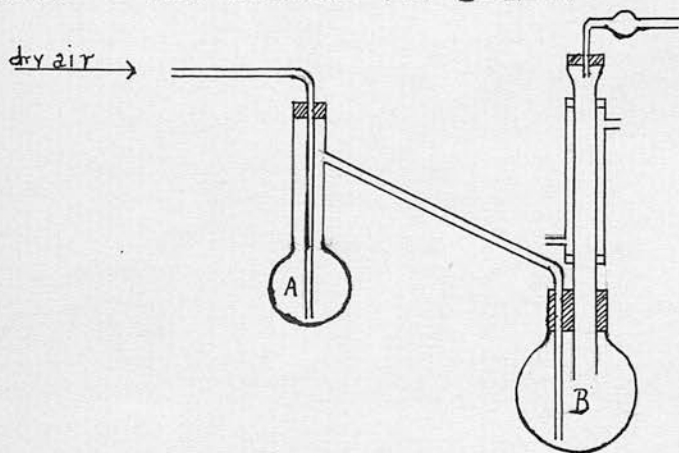
Methyl iodide was added slowly to magnesium filings and ether. When the reaction was complete, a mixture of acetone and ether was added and the whole heated under a reflux condenser for half an hour. The product was cooled, decomposed by the addition of ice, acidified with dilute sulphuric acid, and the volatile liquid distilled. The distillate was subjected to the action of potassium hydroxide and the tertiary-butyl-alcohol so formed, was separated by distillation.

The alcohol was then saturated with hydrobromic acid, when tertiary-butyl-bromide (VII) was obtained. The bromide was washed in turn with water, sodium/

sodium carbonate and water, dried over potassium carbonate and fractionated over phosphorus pentoxide. (compare Perkin, J.pr.Chem., 1885, [2], 31, 498).

m-Tertiary-butyl-toluene (VIII) could not be obtained by the action of ~~bromo~~^{m-bromo}-m-toluene on tertiary-butyl-bromide in presence of magnesium.

A sample of m-tertiary-butyl-toluene, obtained from Schuchardt (Görlitz), was brominated at its boiling point by bromine vapour, in the apparatus shown. The bromine (27 grams)



was contained in the flask A, and a current of dry air, conducted through it, carried the vapour through the toluene (20 grams) contained in B. Hydrogen bromide was evolved. The reaction flask B was fitted with an inlet tube for the bromine, and condenser, in turn fitted with a calcium chloride tube. The benzyl bromide, so formed, was boiled with formic acid (100%) for 25 minutes to remove di- or tribromo-derivative and when cold the bromide was separated, washed in turn with water, sodium carbonate and finally/

finally extracted with ether. The ethereal layer was shaken with sodium bisulphite to remove aldehyde. After evaporation away of the ether, a benzene solution of the impure bromide was saturated with hydrogen bromide to convert any benzyl alcohol to bromide. The benzene solution was dried over calcium chloride in an atmosphere of hydrogen bromide, the benzene distilled away and the bromide fractionated under reduced pressure, using a modification of the Widmer flask. The portion distilling at $124^{\circ} - 126^{\circ}/13$ mm., did not crystallise at -18° , and at -190° it solidified to a glass, which was allowed to become semi-solid and the liquid decanted, with a view to obtaining a partial purification. After this operation, the solid, when molten once more, was found to be impure. The percentage of hydrolysable bromine was low, probably owing to the difficulty of converting the last trace of alcohol (formed during purification) back into bromide. The impure benzyl bromide was therefore gently heated with a slight excess of phosphorus pentabromide and the reaction mixture allowed to stand over night. Hydrogen bromide was evolved. The product was decanted from phosphorus pentabromide and fractionated under reduced pressure, using a modification of the Widmer flask. After a large number of distillations, the main fraction had b.p. $115.5^{\circ}/8$ mm. and did not contain phosphorus, that is, compounds of the/

the type $R \cdot CH_2O \cdot PBr_2$ (compare Boyd and Chignell, J.C.S., 1923, 123, 813) were absent. Found: hydrolysable Br, 34.6. $C_{11}H_{15}Br$ requires Br, 35.25 per cent. In this way 7 grams m-tertiary-butyl-benzyl-bromide were obtained from 88 grams m-tertiary-butyl-toluene, representing a yield of 5 per cent. The loss of material was due to the great precaution taken, to ensure a pure sample being obtained.

The benzyl-bromide is a colourless non-lachrimatory liquid.

p-Tertiary-butyl-benzyl-bromide.

p-Tertiary-butyl-benzyl-bromide was obtained by ^{the} bromination of ~~the~~ p-tertiary-butyl-toluene.

p-Tertiary-butyl-toluene.

p-Tertiary-butyl-toluene was prepared by Verley's method (Bl., 1898, [3], 19, 67). Fuming sulphuric acid (4 parts by weight) ^{was} ~~was~~ added in small quantities to a continually stirred mixture of isobutyl alcohol (one part) and toluene (4 parts) during the course of an hour. Considerable heat was developed, especially towards the end of the reaction. To the reaction mixture water was added and the whole allowed to cool. The liquid consisting of two layers was decanted from the solid, probably toluene p-sulphonic acid which crystallised out at this stage, and to which water was added. Two layers separated and were/

were added to the main liquid, from which the lighter layer was collected and then distilled. The distillate was fractionated and the fraction distilling between 190° and 193° was collected separately. In this way 144 grams p-tertiary-butyl-toluene were obtained from 250 grams isobutyl alcohol, representing a yield of 29 per cent.

p-Tertiary-butyl-benzyl-bromide.

Sixty-nine grams of p-tertiary-butyl-toluene were brominated by the method indicated by Verley, (loc.cit., p.68). Bromine (69 grams) was slowly added to the butyl-toluene at a temperature of 115° . The reaction flask was fitted with a dropping funnel and condenser, in turn fitted with a calcium chloride tube, ^{and} filled with glass beads, to minimise escape of bromine. Hydrogen bromide was evolved. No crystals separated after allowing the benzyl bromide formed, to stand for a few days at 10° . The benzyl bromide was therefore purified in a manner, similar to that by which the meta-isomeride was obtained pure. The portion distilling at $132.5^{\circ} - 134.5^{\circ}/15$ mm. was cooled to -16° and the solid so obtained crystallised from absolute alcohol at -18° . The crystals were immediately filtered and washed with absolute alcohol at the same temperature. Found: hydrolysable Br, 35.3. $C_{11}H_{15}Br$ requires Br, 35.25 per cent. In this way 11.5 grams/

grams p-tertiary-butyl-benzyl bromide were obtained from 144 grams p-tertiary-butyl-toluene, representing a yield of 5 per cent. The loss of material was again due to the great precautions taken, to ensure a good sample being obtained.

The benzyl-bromide is a colourless liquid at ordinary temperatures, b.p. $132.5^{\circ}/14$ mm., with slight lachrimatory properties. It is hygroscopic and darkens on standing. The solid crystallises from absolute-alcohol and petrol ether at -18° in colourless prismatic needles, m.p. $12^{\circ} - 13^{\circ}$. Verley (loc. cit.) does not describe this compound fully and states that it cannot be distilled without decomposing. He did not obtain it in the crystalline condition.

o-Tertiary-butyl-benzoic acid.

An attempt was made to obtain o-tertiary-butyl-benzoic acid from o-bromo-tertiary-butyl-benzene, by the action of carbon dioxide on its magnesium double compound, and subsequent decomposition of the product. Tertiary-butyl-benzene was brominated in presence of iodine, with a view to obtaining o-bromo-tertiary-butyl-benzene, but the para-compound could only be isolated. Kozak (Centr., 1907, I, 1787) claims to have ^{obtained} a mixture of both isomerides.

It was not found possible to prepare the ortho-acid by hydrolysis of the corresponding nitrile, as a satisfactory sample of the latter compound could not be obtained from the o-amino-derivative by means of Sandmeyer's reaction. Diazotisation was carried out/

out in dilute hydrochloric acid solution, and again the operation proved to be difficult, as the diazonium-compound decomposed rapidly at 0° . The diazotisation was therefore carried out at -10° and vigorous stirring resorted to.

The acid was finally obtained by the action of carbon dioxide on the double compound formed by the action of magnesium on o-iodo-tertiary-butylbenzene. Two grams o-iodo-tertiary-butylbenzene were dissolved in dry ether (8 c.c.) and magnesium (0.18 gram) along with a crystal of iodine added. The reaction flask was fitted with a condenser, in turn fitted with a calcium chloride tube. A reaction commenced after slight warming of the flask, and continued at ordinary temperatures. It was completed on the steam-bath, and carbon dioxide was passed into the viscous reaction mixture, cooled in ice, for 4 hours. (It was found that the use of solid carbon dioxide was not so satisfactory). The yield was not increased by gently heating the reaction flask after the carbon dioxide had been passed in for 3.5 hours. The product was decomposed by careful addition of ice, followed by dilute hydrochloric acid. The ortho-acid, so obtained, was extracted with ether, the ethereal layer washed with water and shaken up with sodium carbonate. ^{Concentrated} Hydrochloric acid in excess was added to the sodium carbonate extract, when o-tertiary-butyl/

butyl-benzoic acid was precipitated. The acid was extracted with ether, and after evaporation away of the ether, was recrystallised from hot water, when the plates so obtained, had m.p. 67.5° – 68° . 0.9 gram of o-tertiary-butyl-benzoic acid was obtained from 8 grams o-iodo-tertiary-butyl-benzene, representing a yield of 16 per cent. An analysis of the compound resulted as follows. Found: C, 73.8; H, 7.8. $C_{11}H_{14}O_2$ requires C, 74.2; H, 7.9 per cent.

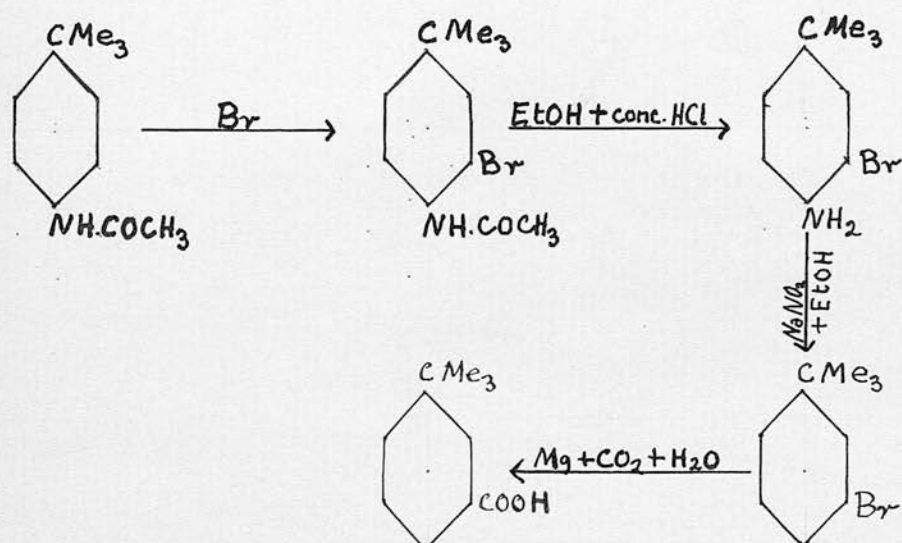
m-Tertiary-butyl-benzoic acid.

m-Tertiary-butyl-benzoic acid was obtained by heating m-tertiary-butyl-benzyl bromide with an aqueous solution of potassium permanganate (4 per cent) under a reflux condenser, until the colour of the permanganate had disappeared. Sulphur dioxide was passed into the reaction product, which was extracted with ether. The ethereal layer was washed with aqueous sodium hydroxide, from which the acid was precipitated with dilute hydrochloric acid. The acid was recrystallised from boiling water, when the white plates, so obtained, had m.p. 127° . [Kelbe and Pfeiffer (Ber., 1886, 19, 1725*) give 127°]

A further quantity of m-tertiary-butyl-benzoic/

* The m-isobutyl-benzoic acid described in this reference is really m-tertiary-butyl-benzoic acid.

benzoic acid was prepared by the action of carbon dioxide on the double compound formed by the action of magnesium on m-bromo-tertiary-butyl-benzene. The full synthesis is summarised as follows:-



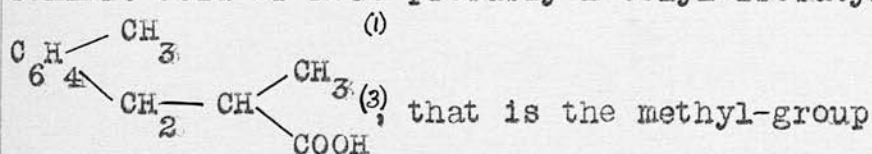
m-Brom-tertiary-butyl-benzene was prepared by a method similar to that used for the preparation of m-bromo-toluene (vide page 40). Excess bromine was added to a vigorously stirred solution of p-acetamino-tertiary-butyl-benzene (10 grams) in glacial acetic acid, the stirring being continued for half an hour after the last addition, which was so regulated that the temperature was maintained at/

at 50°- 55°. The reaction mixture was poured into a large quantity of water containing sodium bisulphite to remove bromine, when 3-bromo-4-acetamino-tertiary-butyl benzene* was precipitated as a white solid, which was filtered, and washed with water. After recrystallising from alcohol, the plates, so formed, had m.p. 156°- 158° (Gelzer, loc.cit., gives 153°). Sixteen grams were obtained, from which 8 grams of 3-bromo-4-amino-tertiary-butyl-benzene* were formed on hydrolysis with ethyl alcohol and concentrated hydrochloric acid. The amine was diazotised with sodium nitrite (4 grams) in 7 c.c. water, in presence of a mixture of ethyl alcohol (21 c.c.) and concentrated sulphuric acid (5 c.c.). During ^{the} diazotisation the temperature was maintained below 10°. The diazo-compound was decomposed by heating carefully with copper powder on the steam-bath, the m-bromo-tertiary-butyl-benzene*, so formed, purified as described for m-bromo-toluene (page 41). Four grams were obtained, from which the meta-acid was prepared, in a manner similar/

* This compound is described by Gelzer (Ber., 1888, 21, 2941 et seq.) as the corresponding isobutyl-derivative.

similar to that by which the ortho-acid was obtained from o-iodo-tertiary-butyl-benzene. This method leaves no doubt that the constitution of the acid so obtained is $\text{Me}_3\text{C} \cdot \text{C}_6\text{H}_4 \cdot \text{COOH}$. It is identical with the acid prepared by the oxidation of m-tertiary-butylbenzyl bromide by potassium permanganate, since a mixture of the two samples had m.p. 127° .

It appeared necessary to prove the constitution of the acid obtained in the latter case, since Kelbe (Ber., 1883, 16, 620) isolated an acid m.p. $91^\circ - 92^\circ$ from the action of dilute nitric acid on m-isobutyl-toluene* and stated that it was either m-isobutylbenzoic acid or more probably m-tolyl-isobutyric acid,

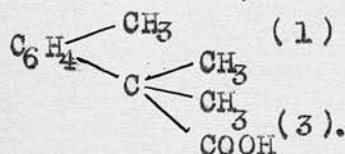


attached to the benzene ring had not been oxidised.

Again Effront (Ber., 1884, 17, 2330) claims to have obtained m-tolyl-propionic acid $\text{C}_6\text{H}_4 \begin{array}{l} \text{CH}_3 \\ \text{CH}_2 \end{array} \cdot \text{CH}_2 \cdot \text{COOH}$ (3)

by the oxidation of m-isobutyl-toluene** with dilute nitric acid and gives its m.p. as 125° , which is very similar to that of m-tertiary-butylbenzoic acid, m.p. 127° . It is very doubtful, however, whether the acid obtained by Effront has the constitution he suggests,

and/ * This is in reality m-tertiary-butyl-toluene, and hence the acid could not have had the constitution quoted by Kelbe, but might have had an analogous constitution, that is, m-tolyl-dimethyl-acetic acid,



** This is really m-tertiary-butyl-toluene as before.



and it was probably *m*-tertiary-butyl-benzoic acid, since Kelbe and Pfeiffer (loc.cit.) later describe the acid, m.p. 127° , resulting from *m*-isobutyl-toluene (really *m*-tertiary-butyl-toluene) and dilute nitric acid as *m*-isobutyl-benzoic acid, that is, *m*-tertiary-butyl-benzoic acid.

p-Tertiary-butyl-benzoic acid.

The acid was prepared by the oxidation of *p*-tertiary-butyl-benzyl bromide or *p*-tertiary-butyl-toluene (vide Verley, loc.cit. p. 71). The bromide or toluene was heated under a reflux condenser with nitric acid (D, 1.20) for 6 hours, when the acid so formed was filtered and dissolved in hot aqueous sodium hydroxide. Unchanged benzyl bromide or toluene was extracted away with ether and the acid precipitated from the alkaline aqueous layer with dilute hydrochloric acid, and purified by means of animal charcoal in boiling alcohol, from which it crystallises in rhombic prisms (compare Bialobrzewski, Ber., 1897, 30, 1775), m.p. 164.5° - 165° . [Verley gives 164° ; Kelbe and Pfeiffer (loc.cit.^{*}) 164° ; Bialobrzewski (loc.cit.) 164° ; Pahl (Ber., 1884, 17, 1237^{*}) 161°]. It is insoluble in cold, but sparingly soluble in hot water.

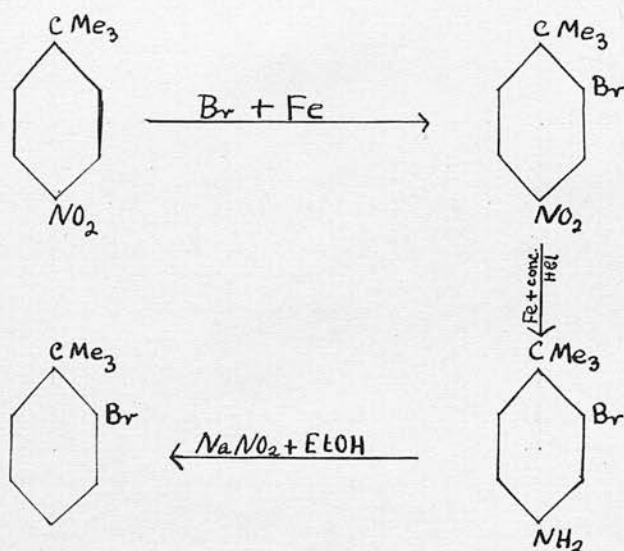
The same acid was obtained by the action of carbon/

*The *p*-isobutylbenzoic acid described in this reference is really *p*-tertiary-butyl-benzoic acid.

carbon dioxide on the magnesium compound of p-bromo-
 tertiary-butyl-benzene (compare the preparation of
 o-tertiary-butyl-benzoic acid, p.46).

o-Bromo-tertiary-butyl-benzene.

o-Bromo-tertiary-butyl-benzene was obtained
 by means of the following series of reactions:



2-Bromo-4-nitro-tertiary-butyl-benzene.

2-Bromo-4-nitro-tertiary-butyl-benzene was
 prepared by heating p-nitro-tertiary-butyl-benzene
 (6 grams, ^{one molecule}) with bromine (7.2 grams, 1.8 molecules) in
 presence of finely divided iron (1.2 grams) in a
 flask fitted with a condenser, in turn fitted with a
 calcium chloride tube, for 7 hours at 90°*. [Ferrous
 bromide, used by Scheufelen (Annalen, 1885, 231, 171) in
 the bromination p-nitro-toluene, and also an aluminium-
 mercury couple were found to be unsatisfactory catalysts.]

Hydrogen/

*It is interesting to note that in the
 bromination of p-nitro-toluene, using iron as
 catalyst, the operation may be performed at 70°
 and completed within 5 hours.

Hydrogen bromide was evolved. When cold, the reaction product formed a semi-solid mass, which was distilled in a current of superheated steam. An oil distilled over, which slowly crystallised in the condenser and receiver to a yellow oily solid. The solid was filtered off, washed with water and pressed well on a porous tile. It crystallised from alcohol in large colourless needles, and had m.p. 93° - 94° . Found: Br, 30.1.

$C_{10}H_{12}NO_2Br$ requires Br, 31.0 per cent. In this way 14.5 grams 2-Bromo-4-nitro-tertiary-butyl-benzene were obtained from 38 grams p-nitro-tertiary-butyl-benzene, representing a yield of 27 per cent. There was however an oil (chiefly unchanged nitro-compound) remaining after filtration off of the solid, which amounted to 26.5 grams. This meant, therefore, that only 11.5 grams p-nitro-tertiary-butyl-benzene had been used and the yield of the bromo-compound was about 88 per cent of that expected.

2-Bromo-4-amino-tertiary-butyl-benzene.

2-Bromo-4-nitro-tertiary-butyl benzene was reduced to the corresponding amino-derivative by West's method (J.C.S., 1925, 127, 494). Concentrated hydrochloric acid (one c.c.) was added to a solution of the nitro-compound (7.5 grams) in 30 c.c. alcohol, and the mixture heated under a reflux condenser to boiling, when finely divided iron (5 grams) was added in 4 portions, allowing 5 minutes to elapse between/

between each addition. During the addition of iron, the reaction mixture was boiled vigorously, to prevent the iron from caking, and the heating was continued for 2 hours after the last addition. The product was filtered from iron, which was then washed well with alcohol and the washings added to the filtrate. The amine was precipitated by the addition of water to the filtrate, extracted with ether, the ethereal layer washed with dilute hydrochloric acid, when the hydrochloride was precipitated, which was filtered off and washed with ether. The hydrochloride was dissolved in hot dilute hydrochloric acid and the base precipitated by the addition of an excess of ammonia (D.O.880). The amino-compound did not solidify and was therefore extracted with ether, the ethereal layer dried over sodium sulphate and after evaporation away of the ether, the amine distilled under reduced pressure, when it had b.p. 152.5° - 154.5° /14 mm. Found: Br, 35.1. $C_{10}H_{14}NBr$ requires Br, 35.1 per cent. It is obtained as a pale yellow liquid. In this way 5.5 grams 2-bromo-4-amino-tertiary-butylbenzene were obtained from 9 grams 2-bromo-4-nitro-tertiary-butylbenzene, representing a yield of 69 per cent. The hydrochloride had m.p. 235° (with decomposition).

2-Bromo-4-acetamino-tertiary-butylbenzene was prepared in the same manner as was the acetyl-derivative/

derivative of 2-nitro-4-amino-tertiary-butyl-benzene. It crystallised from aqueous alcohol in oblong tables of m.p. 142° - 143° .

O-Bromo-tertiary-butyl-benzene.

O-Bromo-tertiary-butyl-benzene was prepared by the elimination of the amino-group from 2-bromo-4-amino-tertiary-butyl-benzene. The method employed was similar to that used in the preparation of o-nitro-tertiary-butyl-benzene from the 2-nitro-4-amino-derivative. The diazonium compound was rather unstable and decomposed above -2° . In this way, 2.5 grams o-bromo-tertiary-butyl-benzene, distilling at 95.5° - 97.5° / 15 mm., were obtained from 5 grams of the bromo-amine, representing a yield of 54 per cent. Found; Br, 38.0. $C_{10}H_{13}Br$ requires Br, 37.6 per cent.

EXPERIMENTAL.Reduction of the isomeric iodo-tertiary-butyl-benzenes.

Experiments were first carried out at 25°. Approximately 0.5 gram of the iodo-compound was weighed into a tall stoppered measuring cylinder. Six c.c. of a solution of hydrogen iodide in glacial acetic acid, containing 0.40 gram hydrogen iodide per c.c. were added, the contents of the cylinder were thoroughly mixed, and when the iodo-compound was completely in solution, the cylinder placed in a thermostat at 25°. At stated intervals, one c.c. of the mixture was withdrawn and run into about 100 c.c. of water. The iodine liberated during the reduction was titrated with standard sodium thiosulphate. To eliminate the error in these experiments due to the liberation of iodine by atmospheric oxidation, a blank experiment was performed. The percentage reduction was calculated from the equation:-



The results, represented graphically in Figure I, Page 9, are summarised in Table I, where t is the time in days, from the commencement of the experiment, w the weight of the iodo-compound taken in grams, and x the percentage changed.

Table I/

TABLE I.

o-Iodo-tertiary-butyl-benzene p-Iodo-tertiary-butyl-benzene.

t	W	X	t	W	X
2	0.0791	61	2	0.0809	11
4	0.0791	76	4	0.0809	19
14	0.0791	86	14	0.0809	35

The meta-isomeride was quite stable towards the hydriodic-acetic acid solution; no trace of liberated iodine due to reduction could be detected.

The reductions of the iodo-compounds were also carried out at 100°. A standard solution of the iodo-compound was made by dissolving an accurately weighed amount (approximately 0.5 gram) in 50 c.c. glacial acetic acid in a graduated flask. 10 c.c. of the standard solution of the iodo-compound and 10 c.c. constant boiling hydriodic acid were measured into a 25 c.c. standard stoppered flask, the contents made up to 25 c.c. with glacial acetic acid and well mixed. The flask was immersed in a thermostat at 100° for a definite period of time*, after which, the contents of the flask were diluted with water, and the free iodine titrated with standard sodium thiosulphate. The error due to iodine liberated by atmospheric oxidation was eliminated by carrying out a blank experiment. The percentage reduction was calculated in the usual manner. The results are shown graphically

in/ * A few minutes longer than the time recorded was allowed, in order that equilibration ^{at temperature} may be established.

in Figure II page 10 , and are summarised in Table II, where t is the time in hours from the commencement of the experiment, whilst w and x have the same significance as before.

Table II.

o-Iodo-tertiary-butyl-benzene.

t	w	x
1½	0.1020	14
3	0.1020	27
6	0.1020	46

m-Iodo-tertiary-butyl-benzene			p-Iodo-tertiary-butyl-benzene.		
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t	w	x	t	w	x
6	0.1061	4	6	0.1015	16

The meta- and para-compounds were also reduced at 100°, using a greater concentration of hydriodic acid, that is a stronger reducing agent. Fourteen c.c. constant-boiling hydriodic acid were placed in a 25 c.c. graduated flask, containing 10 c.c. the of standard solution of the iodo-compound, the contents made up to 25 c.c. with glacial acetic acid and thoroughly mixed. The percentage of the iodo-compound reduced after a stated time, was estimated in the usual manner, correction being applied for air oxidation. The results are summarised in Table III, t, w and x having the same significance as in Table II.

Table III.

m-Iodo-tertiary-butyl benzene.

t	w	x
6	0.1061	5

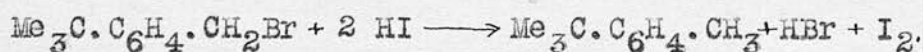
p-Iodo-tertiary-butyl benzene.

t	w	x
6	0.1015	28

Insufficient of the product of reduction of the diiodo-compound at 25° was obtained for identification, but a strong odour of tertiary-butyl-benzene was apparent.

Reduction of m- and p-tertiary-butyl-benzyl bromides.

The action of hydrogen iodide on m- and p-tertiary-butyl-benzyl bromides was examined at 25°. Approximately 0.5 gram of the bromide was weighed into a tall stoppered measuring cylinder and dissolved in 5 c.c. of a solution of hydrogen iodide in glacial acetic acid containing 0.33 gram hydrogen iodide per c.c. The cylinder was immersed in a thermostat at 25°, and at recorded intervals, 1 c.c. of the reduction mixture was withdrawn and the amount of iodine liberated, estimated in the usual manner. A blank experiment was also performed and the amount of the bromide reduced calculated from the equation:-



The results, which are shown graphically in Figure III page 11, are tabulated below (Table IV), where t is the time in days from the commencement of the experiment, w and x having their usual significance.

Table IV.

m-Tertiary-butyl-benzyl-bromide.			p-Tertiary-butyl-benzyl-bromide.		
t	w	x	t	w	x
4	0.0981	10	4	0.0960	8
8	0.0981	16	8	0.0960	12
15	0.0981	20	15	0.0960	15
22	0.0981	21	22	0.0960	17

Benzyl/

Benzyl bromide is only reduced to the extent of approximately 2 per cent (vide Shoesmith and Slater, J.C.S., 1924, 125, 2282) after two days.

The reductions were also carried out at 100°. 10 c.c. of a standard solution of the bromide and 10 c.c. constant-boiling hydriodic acid were placed in a graduated flask, made up to 25 c.c. with glacial acetic acid and the contents mixed. The flask was then placed in a thermostat at 100° and the amount of bromide reduced in a definite time was estimated, as before, a blank experiment being also performed. The results are shown graphically in Figure IV page 12, and are summarised in Table V., where w and x have the same significance as in previous experiments, whilst t is the time in hours from the commencement of the reduction. $K_{u,100^\circ}$, $K_{m,100^\circ}$ and $K_{p,100^\circ}$ are the approximate velocity constants for benzyl bromide and m- and p-tertiary-butyl-benzyl bromides respectively.

TABLE V..

m-Tertiary-butyl-benzyl bromide.			p-Tertiary-butyl-benzyl bromide.		
t	w	x	t	w	x
1½	0.1031	37	1½	0.1014	28
3	0.1031	54	3	0.1014	41
6	0.1031	71	6	0.1014	57

$$K_{u,100^\circ} = 0.20;^* \quad K_{m,100^\circ} = 0.39; \quad K_{p,100^\circ} = 0.23.$$

* (Shoesmith and Slater, J.C.S., 1926, 217).

The bromides were reduced in a similar manner with constant-boiling hydriodic acid at 110° in the vapour thermostat described below. The results are represented graphically in Figure IV page 12 and summarised in Table VI in which t , w and x have the same significance as in Table V. $K_{u_{110^{\circ}}}$, $K_{m_{110^{\circ}}}$ and $K_{p_{110^{\circ}}}$ are also given.

Table VI.

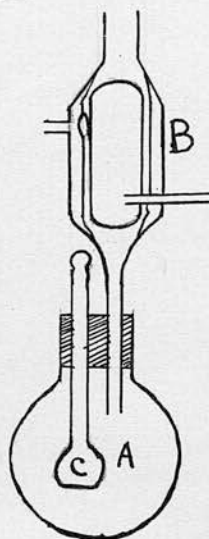
m-Tertiary-butyl-benzyl
bromide

p-Tertiary-butyl-benzyl
bromide.

t	w	x	t	w	x
$1\frac{1}{2}$	0.1012	58	$1\frac{1}{2}$	0.1038	48
3	0.1012	79	3	0.1038	70
6	0.1012	97	6	0.1038	93

$$K_{u_{110^{\circ}}} = 0.39^*; \quad K_{m_{110^{\circ}}} = 0.87; \quad K_{p_{110^{\circ}}} = 0.63.$$

The vapour thermostat.



The vapour thermostat, shown diagrammatically above, consists of a flask A of 500 c.c. capacity, fitted/

* Shoesmith and Slater (loc.cit.).

fitted with a double bored stopper, carrying a double surface condenser B and a 25 c.c. standard flask C. A liquid which boils at the desired temperature is placed in A and heated to boiling, when C, containing the particular reaction mixture, is immersed in the vapour from the boiling liquid for the stated interval of time. The flask C soon attains the temperature of the vapour, but it is advisable to allow a few minutes longer than the specified time, in order that equilibration of temperature may be established. Suitable liquids for A are chloroform, b.p. 60° , carbon tetrachloride, b.p. 76° and toluene, b.p. 110° . Isolation and identification of the reduction product from p-tertiary-butyl-benzyl bromide.

p-Tertiary-butyl-benzyl bromide (1.5 grams) was placed in a tall stoppered measuring cylinder and dissolved in 15 c.c. of a solution of hydrogen iodide acid in glacial acetic acid containing 0.40 gram hydrogen iodide per c.c. The cylinder was placed in a thermostat at 25° for 10 days, after which, the reaction product was poured into 500 c.c. water, containing sodium thiosulphate, to destroy free iodine. The solid which separated was filtered, washed with water and recrystallised from dilute acetic acid. The colourless plates, so obtained, had m.p. 29.5° - 30.5° . In order to identify the reduction product, p-tertiary-butyl-benzyl iodide was prepared by heating p-tertiary-butyl/

butyl-benzyl bromide (2 grams) in acetone solution with potassium iodide (1.5 grams) under a reflux condenser for several hours. The product was poured into water, the solid obtained, filtered and washed with water. It crystallised from dilute acetic acid in colourless plates, when it had m.p. 28.5° – 29.5° . One gram was obtained. Found: hydrolysable I, 46.0. $C_{11}H_{15}I$ requires I, 46.3 per cent. Mixed m.p. with the sample obtained from the reduction with hydriodic acid, 29.5° – 30° .

Hydrolysis of m- and p-tertiary-butyl-benzyl bromides.

The first hydrolyses were carried out at 60° , in aqueous alcoholic solution. Approximately 0.1 gram of the bromide was weighed into a 25 c.c. graduated flask, dissolved in 20 c.c. absolute alcohol, 5 c.c. water added, the contents of the flask well mixed, and then made up to 25 c.c. with absolute alcohol. The stoppered flask was heated at 60° in the vapour thermostat for specified periods of time, after which the contents of the flask were diluted with water and the hydrobromic acid, formed during hydrolysis, titrated with N/20 ammonia, using methyl red as indicator. The percentage hydrolyses were calculated from the equation $Me_3C.C_6H_4.CH_2Br + HOH \rightarrow Me_3C.C_6H_4.CH_2OH + HBr$. The results are summarised in Table VII, where t is the time in hours from the commencement of the experiment, w the weight of bromide taken in grams, and/

and x the percentage changed. The results are represented graphically in Figure V page 13. $K_{u_{60^\circ}}$, $K_{m_{60^\circ}}$, $K_{p_{60^\circ}}$, are the reciprocals of the times required for half-completion of the hydrolysis of benzyl bromide, ~~and~~ m - and p -tertiary-butyl-benzyl bromides respectively.

TABLE VII.

m -Tertiary-butyl-benzyl bromide			p -tertiary-butyl-benzyl bromide.		
t	W	X	t	W	X
$\frac{1}{2}$	0.1024	30	$\frac{1}{2}$	0.1192	44
1	0.1460	48	1	0.1196	71
2	0.1072	70	2	0.1141	86
4	0.1131	86	4	0.1296	95
8	0.1103	95	8	0.1033	99

$$K_{u_{60^\circ}} = 0.67; \quad K_{m_{60^\circ}} = 0.95; \quad K_{p_{60^\circ}} = 1.41.$$

A perfectly satisfactory velocity constant could not be obtained at 60° owing to the rapidity of hydrolysis, and consequently the hydrolyses of the bromides were carried out at 25° . Approximately 0.5 gram of the bromide was weighed into a 100 c.c. graduated flask and 90 c.c. absolute alcohol followed by 10 c.c. water added and the contents well mixed, after which they were made up to 100 c.c. with absolute alcohol. The flask was placed in a thermostat at 25° and 10 c.c. of the contents were withdrawn at stated intervals, diluted with water, and the hydrobromic acid present, titrated rapidly with $N/20$ NaOH and methyl red. The percentage hydrolyses were calculated in the usual manner. The hydrolyses were sufficiently slow to allow/

*Shoesmith and Slater (loc.cit.).

allow satisfactory velocity constants to be obtained. The results are summarised in Table VIII in which t , w and x have the same significance as before and k_{25}° is the velocity constant, calculated from the unimolecular formula:

$$k = \frac{2.3}{60 \times t} \log_{10} \frac{a}{a - x},$$

where a represents complete hydrolysis. The velocity constant for unsubstituted benzyl bromide is $k_{u25}^{\circ} = 125 \times 10^{-6}$ * and it was found that for the meta-isomeride, $k_{m25}^{\circ}(\text{mean}) = 192 \times 10^{-6}$, and for the para-isomeride, $k_{p25}^{\circ}(\text{mean}) = 333 \times 10^{-6}$.

Table VIII.

m-Tertiary-butyl-benzyl bromide.

t	w	x	$k_{m25}^{\circ} \times 10^6$
36	0.0518	33.7	190
47	0.0518	41.9	192
54	0.0518	46.6	193

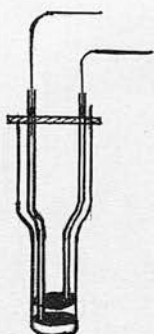
p-Tertiary-butyl-benzyl bromide.

t	w	x	$k_{p25}^{\circ} \times 10^6$
36	0.0500	51.4	334
54	0.0500	66.4	336
60	0.0500	69.5	329

*Shoosmith and Rubli (loc.cit.).

Dissociation constants of the isomeric tertiary-butyl-
benzoic acids.

These were estimated by the usual Kohlrausch conductivity method, using a cell of the type shown. It was found that satisfactory results could only be obtained when the cell electrodes were small and almost one cm. apart.



Owing to the insolubility of the meta- and para-isomerides, saturated solutions of which had concentrations of approximately $N/2000$ and $N/3500$ respectively and the unreliability of observations with dilutions greater than those recorded, it was decided to find the dissociation constants at one dilution only for all three acids, namely, approximately $N/3500$, this being the limiting solubility of the para-acid. The dissociation constant of the ortho-acid was found at this dilution in order that a true comparison might be made. The acids were recrystallised several times before the dissociation constants were determined. The acid (0.5 gram) was shaken up with conductivity water (250 c.c.) for 2 days in a well stoppered Jena glass bottle*, the solution/

*All vessels containing solutions whose conductivities were to be measured were very carefully cleaned before use by subjecting them to the action of steam for 5 minutes.

solution being periodically placed in a thermostat at 25°. The solution at 25° was filtered through glass wool into another Jena glass bottle, which was then placed in the thermostat. Filtering through glass wool did not affect the conductivity of the solution; provided the glass wool had been well washed with conductivity water, and as the filtering medium enabled the operation to be performed expeditiously, the solution was not exposed to the atmosphere for such time as to increase the conductance of the solution appreciably. The strength of the saturated solutions of these acids at 25° was estimated by titration with N/140 baryta solution and was N/96, N/2246, N/3646 for the ortho-, meta- and para- acids respectively. The solution of the ortho-acid was diluted to approximately N/3000, for reasons stated before. Ten c.c. of the solution were withdrawn and placed in the cell. (As minute particles of undissolved acid were still present in the liquid, the solution was passed through glass wool, before entering the pipette). After 5 minutes, when equilibration of temperature had been established, the resistance of the solution was determined with two or more different resistances in the resistance box. The molecular conductivity at this dilution, $\mu\phi$ was then calculated from the formula:

$$\mu\phi = \frac{C\phi}{R} \cdot \frac{x}{100-x},$$

where C is the cell constant,* ϕ the volume in c.c. in/

*The cell constant was determined, using N/50 potassium chloride, and found to be 0.5907.

in which 1 gram-molecule is dissolved. R is the resistance in the resistance box and x the bridge reading in cm. It was then required to determine the molecular conductivities of the acids at infinite dilution. Since the molecular conductivity at infinite dilution of isomeric acids are equal (vide White and Jones, Amer. Chem. J., 1910, 44, 162), it was only necessary to find the molecular conductivity at infinite dilution for one acid. As the tertiary-butyl-benzoic acids are very weak, their molecular conductivities at infinite dilution cannot be satisfactorily determined directly, but ^{it was thought that they might} ~~may~~ be obtained from the equation:

$$\mu_{\infty}(\text{HX}) = \mu_{\infty}(\text{HCl}) + \mu_{\infty}(\text{NaX}) - \mu_{\infty}(\text{NaCl}),$$

where x is the radical $\text{Me}_3\text{C} \cdot \text{C}_6\text{H}_4 \cdot \text{COO}$ and μ_{∞} is the molecular conductivity at infinite dilution. The molecular conductivities at infinite dilution for hydrochloric acid and its sodium salt are known and for sodium tertiary-butyl-benzoate may be found directly. An attempt was therefore made to determine the molecular conductivity at infinite dilution for sodium p-tertiary-butyl-benzoate. The sodium salt was prepared by adding 10 per cent alcoholic sodium hydroxide to an excess of a solution of the para-acid in alcohol. After evaporation away of the alcohol, the sodium salt was washed well with alcohol and ether to extract excess acid and dried. An N/32 solution of/

of the sodium salt was prepared, 5 c.c. of which were placed in the conductivity cell and the resistance of the solution measured. The solution was then diluted in the usual manner and its molecular conductivity estimated, but at high dilutions its molecular conductivity gradually increased and hence μ_{∞} could not be obtained in this way. This is probably due to the hydrolysis of the sodium salt, when the presence of sodium hydroxide would increase the conductivity. The molecular conductivity was ultimately calculated by the application of the rule, formulated by Ostwald, that the molecular conductivity at infinite dilution is the same for acids with the same number of atoms in the molecule. The following table, showing the limiting conductivities of acids which contain 12 or more atoms in their molecule is quoted from Ostwald-Luther, Physiko-Chemische Messungen, Leipzig 1910, p.482.

Table IX.

At 25° the limiting value for

Acids with 12 atoms	μ_{∞}	= 376
" " 15 "	μ_{∞}	= 373
" " 18 "	μ_{∞}	= 371
" " 22 "	μ_{∞}	= 369
" " 25 "	μ_{∞}	= 368
" " 30 "	μ_{∞}	= 367

The tertiary-butyl-benzoic acids have 27 atoms in their molecule/

molecule and hence μ_{∞} at $25^{\circ} = 368$.

From the conductivities at $N/3000$ and the above value for μ_{∞} , α , the degree of ionisation at dilution ϕ , $= \frac{\mu_{\phi}}{\mu_{\infty}}$ and the dissociation constant $k = \frac{\alpha^2}{(1-\alpha)v}$ was determined, where v is the volume in litres containing one gram-equivalent. It is more convenient to take the dissociation constant as $K = 100 \cdot k$, owing to the small magnitude of k . The results are summarised in Table X., the dissociation constant of benzoic acid, $K_{u_{25^{\circ}}}$, being quoted for comparison.

Table X..

o-Tertiary-butyl-benzoic acid.

μ_{ϕ}	α	$k \times 10^2$
205.8	0.5594	2.8

<i>m</i> -Tertiary-butyl-benzoic acid			<i>p</i> -Tertiary-butyl-benzoic acid.		
μ_{ϕ}	α	$k \times 10^{-3}$	μ_{ϕ}	α	$k \times 10^{-3}$
106.2	0.2886	5.2	119.0	0.3233	4.2

$$K_{u_{25^{\circ}}} = 6.9 \times 10^{-3}$$

DISCUSSION OF RESULTS.

The results obtained in the investigation present several points for discussion. The main fact which has arisen is that the introduction of the tertiary-butyl-group into a benzene nucleus causes the nucleus to be activated in alternate positions to a marked degree. Observations have been made on compounds containing halogen in the side chain which indicate also increased activation in a general sense, that is, in all positions. Examples of decreased activation due to a steric influence are recorded.

The effects of the various influences are discussed in the following order:

GENERAL EFFECT.

- (1) Hydrolysis of m- and p-tertiary-butyl-benzyl bromides.
- (2) Reduction of m- and p-tertiary-butyl-benzyl bromides.
- (3) Reduction of the isomeric iodo-tertiary-butyl-benzenes.
- (4) Dissociation constants of the tertiary-butyl-benzoic acids.

ALTERNATING EFFECT.

I. Cause of alternation in nuclear reactivity.

- (1) Electron shift.
- (2) Octet stability.

Reduction/

II. Reduction of o- and p-iodo-tertiary-butyl-benzenes.

Possibility of intervention of quinonoid structures.

III. Alternation transmitted through the side chain.

(a) Hydrolysis of m- and p-tertiary-butyl-benzyl bromides.

Cause of this alternation

(1) Electron Shift.

(2) Octet stability.

(b) Reduction of m- and p-tertiary-butyl-benzyl bromides.

(c) Dissociation constants of m- and p-tertiary-butyl-benzoic acids.

STERIC EFFECT.

Abnormality of o-tertiary-butyl-benzoic acid.

CONCLUSION.

The tertiary-butyl-group does not direct substitution in the benzene nucleus in accordance with the simple polarity rule, and in every series of experiments the directing influence of the tertiary-butyl-group has been found to be similar to that of the methyl-group; the ease of removal of halogen from nuclear iodinated derivatives is ortho > para > meta and of removal of side chain halogen by hydrolysing agents para > meta > unsubstituted and by reducing agents meta > para > unsubstituted.

GENERAL/

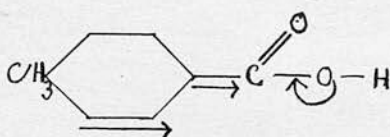
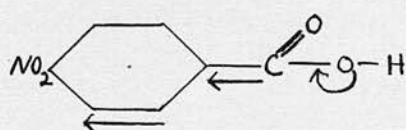
GENERAL EFFECT.

(1) Hydrolysis of m- and p-tertiary-butyl-benzyl bromides.

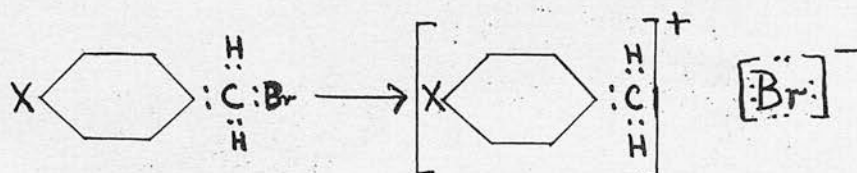
It is not difficult to visualise the factors underlying the general effect, that is, the effect which makes itself apparent in that all the isomerides are more reactive or less reactive than the unsubstituted compound. In the hydrolysis of a compound containing halogen in the side chain, it seems reasonable to suppose that the reactivity of the halogen atom will depend on its power to be eliminated as a negative ion, which will in its turn depend on the accumulation of electrons round the halogen atom. A group which repels electrons towards the halogen will render it more reactive in this sense.

The capacity of a group to repel or attract electrons can be tested in the following way. Ionisation of an organic acid depends on the separation of a proton from the oxygen of the hydroxyl in the carboxyl group. Any factor therefore which assists in pulling the electrons away from the hydrogen will increase ionisation, and vice versa, any group which increases ionisation must attract away electrons from the hydrogen. An example of a group of this nature is to be found in the nitro-group, an "electron sink" and the dissociation constants/

constants of m- and p-nitro-benzoic acids are $K_m = 3.48 \times 10^{-2}$ and $K_p = 4.0 \times 10^{-2}$ at 25° respectively (Ostwald, Z. physikal. Chem., 1889, 3, 241), as compared with benzoic acid, 6.9×10^{-3} at 25° . Meta- and para-toluic acids [dissociation constants 5.6×10^{-3} and 4.3×10^{-3} at 25° respectively (White and Jones, Amer. Chem. J., 1910, 44, 197)] are both weaker than benzoic acid, a fact which is due to the power of the methyl-group to repel electrons, since the effect is the opposite to that in the nitro-benzoic acids (compare Allan, Oxford, Robinson and Smith, J. C. S., 1926, 405). The two cases may be represented graphically as follows, where the curved arrows show the fundamental electron movement which precedes ionisation and the ^{straight} arrow the direction of the secondary effect of the substituent group.



In the hydrolysis of the benzyl bromides, the perfect condition of the bromine separating as a negative ion will never be realised, because that would require the separation of the terminal atom with a negative charge, that is, with one of the carbon electrons. This is very improbable.



The accumulation of electrons in the neighbourhood of the bromine, as a result of repulsion from the methyl-group is however readily visualised and admissable and would render the bromine much more readily attacked by the hydrogen of the hydrolysing agent. The general influence results in all the isomerides being more rapidly hydrolysed than the unsubstituted compound and various attempts have been made to determine the value of this effect (g) from the data obtained from the quantitative hydrolysis of substituted benzyl chlorides and bromides (Shoesmith and Slater, loc. cit., p. 215; van Duin, Rec. trav. Chim., 1927, 46, 262; Berger, ibid 543; Chem. Weekblad, 1927, 24, 61).

The formula used for this purpose is

$$g = \frac{1}{2}(\log_{10} K_m + \log_{10} K_p - 2 \log_{10} K_u), \text{ in}$$

which K_m , K_p , K_u are the velocity constants of hydrolysis of the meta-, para- and unsubstituted compounds respectively (cf. Shoesmith and Slater). The value for g at 25° is 0.31 and at 60° , 0.18; g , calculated for comparison for the methyl-group alone at 60° is 0.34 (the value given in J.C.S., 1926, 217 should be halved) and thus the tertiary-butyl-group is/

is seen to be not so strongly electron repelling as is the methyl-group.

Each methyl-group of the tertiary-butyl-group repels electrons but the effect is not three times as large as in the case of the methyl-group alone, because the influence in the former case is transmitted through an additional carbon atom.

It is also recognised that the value of g is only approximate, since it has been assumed that the general effect is the same ~~in both~~ at the meta- and para-positions, which is improbable.

(2) Reduction of *m*- and *p*-tertiary-butyl-benzyl bromides.

Both these compounds are more rapidly reduced at 110° than is benzyl bromide and $K_{m_{110^\circ}}$, $K_{p_{110^\circ}}$, $K_{u_{110^\circ}}$ have the values 0.87, 0.63 and 0.39 respectively. Thus the value of g calculated as before is 0.28, whilst g for the methyl-group [calculated from observations by Shoesmith and Slater (J.C.S., 1927, 1771)] is 0.52. Again g is markedly positive but less than in the case of the methyl-group.

The greater reactivity of *m*- and *p*-tertiary-butyl-benzyl bromides than the unsubstituted compound towards hydrogen iodide is a phenomenon which is more difficult of explanation than that of the hydrolysis and suggests that there is a stage previous to the actual liberation of iodine, governed by the same/

same factors in the two series. If the decomposition by water and hydrogen iodide is preceded by a loose addition of the reagent at the carbon-bromine linkage, then the initial stages of the two reactions are essentially the same and if none but general influences affected the carbon-bromine linkage, the difference between the reactivity of meta- and para-compounds would be identical, whether water or hydrogen iodide were the reagent. This question however is one to which no satisfactory answer can be given at present.

(3) Reduction of the isomeric iodo-tertiary-butyl-benzenes.

It is noteworthy that whilst the iodine of m-iodo-toluene is slowly removed by hydrogen iodide at 25°, that of m-iodo-tertiary-butyl-benzene is unreactive. This is probably due to the weaker general influence of the tertiary-butyl-group at this point, compared with that of the methyl-group, whilst the slower rate of reduction of p-iodo-tertiary-butyl-benzene than p-iodo-toluene is due to the same cause, since ease of reduction appears to be dependent on the power of a substituent group to act as an electron repeller.

(4) Dissociation constants of the tertiary-butyl-benzoic acids.

The information obtained from the measurement of the dissociation constants of the tertiary-butyl-

butyl-benzoic acids in this connection shows that the general influence of the tertiary-butyl-group is to make the meta- and para- acids weaker than the unsubstituted benzoic acid which again shows that the tertiary-butyl-group is electron-repelling. It is perhaps surprising that the acids do not differ greatly from the corresponding toluic acids, except in the case of the ortho-isomeride. The value of the general effect on the dissociation constants may be calculated from the formula of Flürscheim (J.C.S., 1909, 95, 726) as follows, where p is the general effect (designated the polar effect by Flürscheim), K_m, K_p, K_u are the dissociation constants of the meta-, para- and unsubstituted acids respectively.

$$p = \frac{K_m + K_p}{2K_u} = \frac{5.2 + 4.2}{2 \times 6.9} = 0.68.$$

The value of p , calculated from the constants of the toluic acids is 0.72. This formula differs from that used for the hydrolysis experiments in that the logarithm of the value is used in the latter case.

ALTERNATING EFFECT.

The effect of an alternating influence due to the tertiary-butyl-group is apparent in five instances, namely, (1) direct substitution with nitric acid gives ortho- and para-compounds (Seńkowski, Ber., 1890, 23, 2414), (2) the reduction of o- and p-iodo-tertiary/

tertiary-butyl-benzenes and non-reduction of the meta-isomeride at 25° and 100° , (3) the more rapid hydrolysis of p-tertiary-butyl-benzyl bromide as compared with the meta, (4) the reversal of this order of reactivity in hydriodic acid and (5) the higher dissociation constant of m-tertiary-butyl-benzoic acid than that of the para-isomeride.

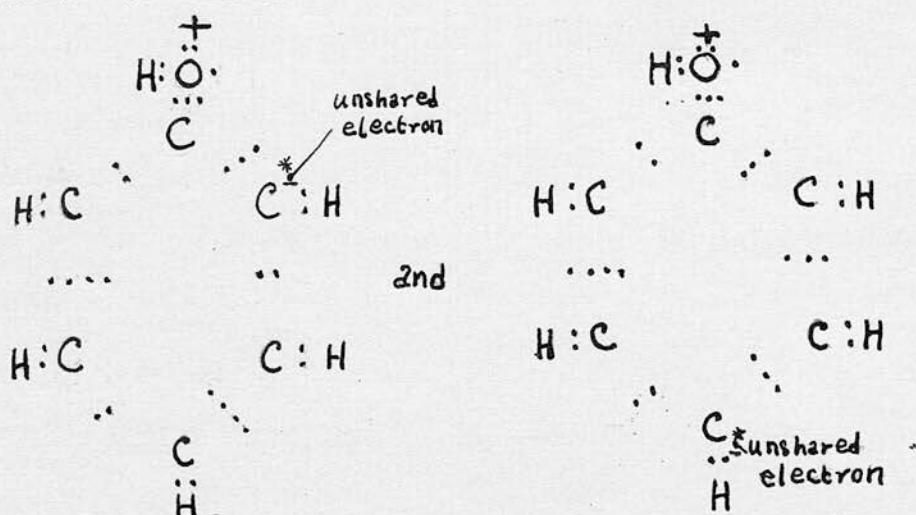
The proof, in this investigation, of the constitution of o-nitro-tertiary-butyl-benzene, obtained by Senkowski (loc.cit.) shows very clearly that the ortho-position is reactive and that it is the great-steric influence of the tertiary-butyl-group which results in the production of a preponderating quantity of the para-isomeride. The reactivity of the ortho-position, both towards nitric acid and bromine, when the para-position is occupied has also been demonstrated, but it is to be remembered in these experiments that the nitro-group itself may have an appreciable influence in directing the third group meta to itself. It was possible to show however that the large hindering effect of the tertiary-butyl-group could be counteracted and provided a means of obtaining ortho-derivatives.

I. Cause of alternation in nuclear reactivity.

(1). Electron shift.

The similarity of the directive influence of the tertiary-butyl-group to that of the hydroxyl-group/

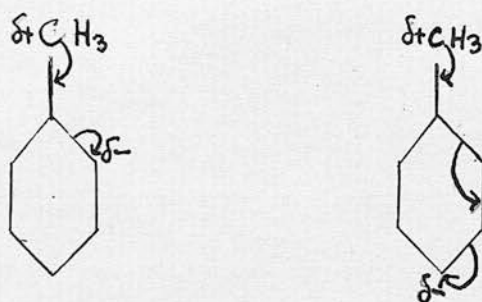
group in phenol necessitates the consideration of the possibility of electronic movement of the type quoted in the introduction (page 2). If an electron source, such as the hydroxyl-group, is present in a benzene nucleus and the molecule is attacked by nitric acid, then the polarisation of the ortho- and para-positions, at the moment of reaction, will take place, as already shown, the oxygen atom originating the electronic shift. The full representation of a phenol molecule when attacked would be as follows:



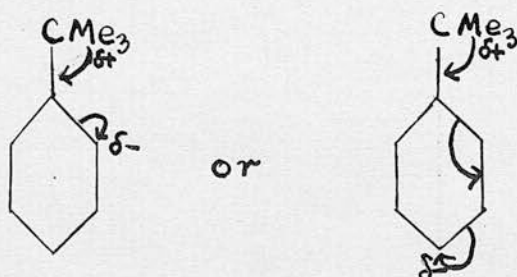
The difficulty arises, however, as to how the tertiary-butyl-group can act as an electron source. Ingold and Ingold (J.C.S., 1926, 1310) have extended Robinson's ideas and regard the direction by methyl*,

*In this connection, it is noteworthy that in the presence of aluminium chloride, toluene and tertiary-butyl-chloride give m-tertiary-butyl-toluene (compare page 39). It is suggested that here the unexpected directing influence of the substituent group is due to association of the catalyst with the methyl-group in a manner similar to that suggested by Olivier in a parallel case (Rec. trav. chim., 1926, 45, 710; *ibid.*, 1927, 46, 605). This problem requires further investigation.

a similar case to the one under discussion, to be due to a slight change in the disposition of the electrons round the carbon atom with production of the same effects as in phenol, but in a lesser degree. This results in small charges denoted by $\delta+$ and $\delta-$ in the former, as opposed to $+$ and $-$ in the latter case appearing in the positions indicated.



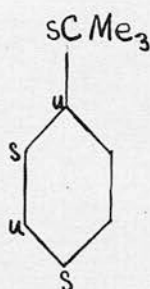
The tertiary-butyl-group must act in the same manner and the reactive molecule will have the form denoted:



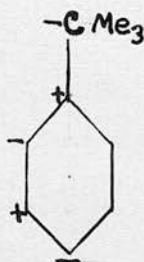
(2) Octet stability.

The reason why the tertiary-butyl-group brings about the polarisation of the ortho- and para-positions would also be readily explicable by the theory of Kermack and Robinson (J.C.S., 1922, 121, 427). This/

This postulates a stable electronic octet (such as would be expected to be present in the tertiary-butyl-group) as the origin of the influence, producing alternating unstable and stable octets which results in the formation of positively and negatively polarised positions. This is formulated as follows where s represents stable and u unstable octets.



The carbon atoms round which are the stable octets in ortho- and para-positions would be negatively polarised,

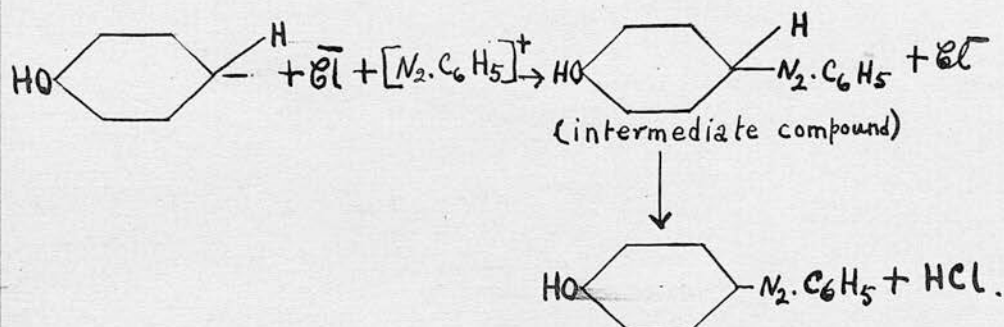


and would be the positions of attack with nitric acid or bromine. This hypothesis is the most attractive from the viewpoint of the present observations, especially when discussed in connection with the order/

order of ease of hydrolyses and reduction of the tertiary-butyl-benzyl bromides (vide later). Thus either mechanism results in the production of negatively polarised ortho- and para-carbon atoms, the positions of attack by reagents, a remark which also applies to the next section of the discussion.

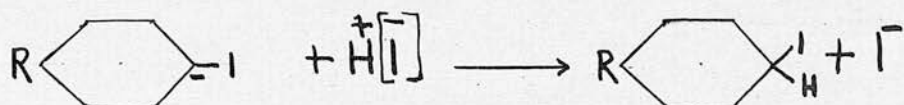
II. Reduction of o- and p-iodo-tertiary-butyl-benzenes.

The removal of iodine from the iodo-tertiary-butyl-benzenes is a phenomenon closely related to that of substitution in the benzene nucleus. A parallel might be drawn between this and ^{diazot-}coupling, when the diazonium compound reacts in virtue of its positive ion and ionises to $[C_6H_5N_2]^+ + Cl^-$. The hydrogen in the attacked position is then expelled as a proton and enters into combination with the chlorine ion, that is,



Reduction/

Reduction of o- and p-iodo-tertiary-butyl-benzenes with hydrogen iodide could correspondingly be formulated in the following way:

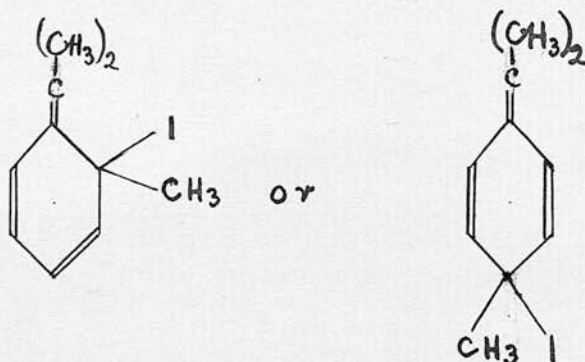


At this stage the greater attraction of ^{the}negatively polarised carbon atom for hydrogen than for iodine results in the expulsion of the latter to a receptor, the negative iodine ion. The great concentration of the hydriodic acid, coupled with the aversion of the benzene nucleus to be directly substituted by iodine, assists the reaction in a forward direction. The polarisation of the ortho-position in this reaction must be very large, as it completely masks the steric hindrance of the tertiary-butyl-group and the rate of reduction at 25° is almost identical with that of o-iodotoluene.

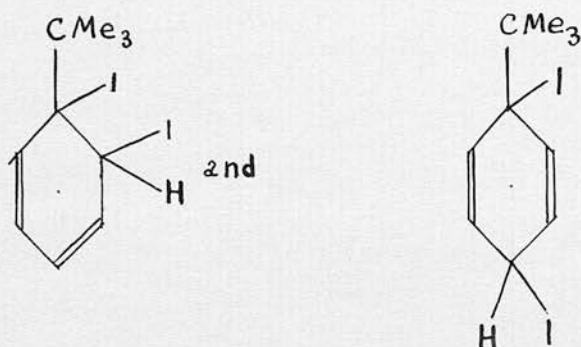
Possibility of intervention of quinonoid structures.

In previous experiments, halogen present in a substituted benzene or naphthalene nucleus has proved to be very reactive (Shoesmith, Hetherington and Slater, J.C.S., 1924, 125, 1314; Shoesmith and Rubli, J.C.S., 1927, 3098) and it appears as if the tendency to react in a quinonoid modification is one of the causes underlying the great reactivity. That removal of iodine/

iodine does not depend solely on such changes is to be concluded from observations from the present research, since it is very improbable that tertiary-butyl-derivatives would react in such a form as would entail the production of molecules of the type,



It may be that addition of the whole molecule of hydrogen iodide precedes substitution, that is,



with subsequent elimination of iodine, which would account for the great reactivity of o-iodo-tertiary-butyl-benzene, but that is a problem for further examination.

III. Alternation transmitted through the side chain.

(a) Hydrolysis/

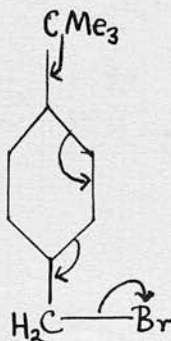
(a) Hydrolysis of *m*- and *p*-tertiary-butyl-benzyl bromides.

The difference in the rates of hydrolysis of *m*- and *p*-tertiary-butyl-benzyl bromides is due to the effect of two influences, namely a general and an alternating influence. The effect of the former has already been discussed (vide page 74). The greater activity of the para-isomeride towards aqueous alcohol is definitely due to the latter, since it is to be expected that the general influence would not be so effective in the para- as in the meta-position; the distance between the influenced and influencing group is greater in the para-compound than in the meta-isomeride.

Cause of this alternation.

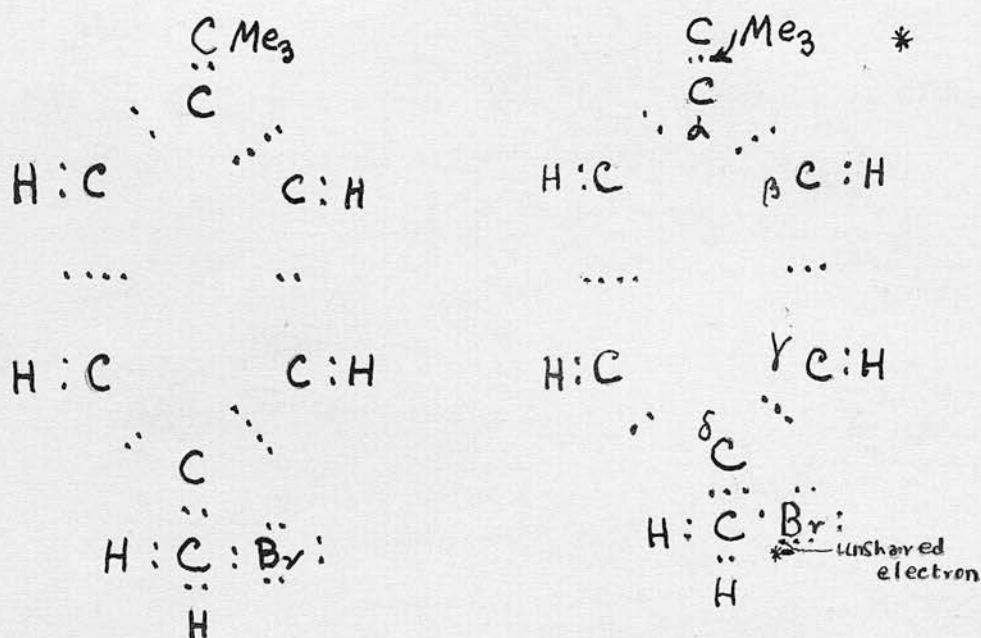
(1) Electron shift.

The shift of electrons which results in the activation of the ortho- and para-positions in nuclear substitution and also in the replacement of iodine by hydrogen could be continued in the case of *p*-tertiary-butyl-benzyl bromide as follows:



This means that as a result of the alternating influence/

influence (superimposed on the general), there is an additional tendency for the bromine atom to become negatively charged at the moment of reaction, because there is a group of the necessary type (an electron source) in the correct position (ortho or para) which will permit the electronic shift. Interpreted in terms of electrons the figure above becomes the following:

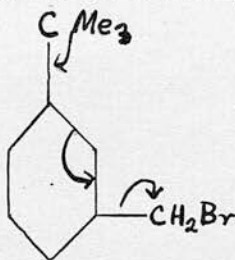


This would be the ideal state, not often reached although examples of a very reactive bromine atom are to be found in p-methoxy-benzyl bromide (Lapworth and Shoesmith J.C.S., 1922, 121, 1394) and 4-methoxy- α -naphthyl-methyl bromide (Shoesmith and Rubli, loc.cit.,

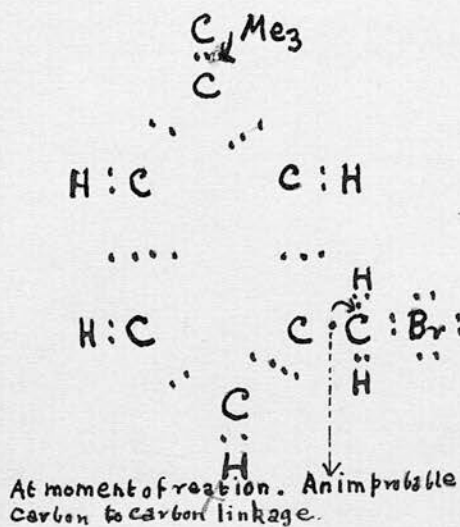
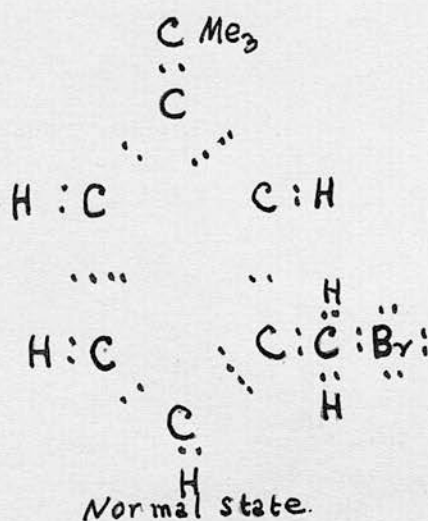
p. 3099/ *In this and similar figures the α -carbon atom in tert.-butyl-compounds is for convenience presented as surrounded by seven electrons. The arrow at this point denotes the counteracting of this deficiency because of the capacity of the tert.-butyl-group to function as an electron source.

p.3099).

The electron shift however does not appear probable as an activator or deactivator of the meta-position, because when the electronic representation is examined it would require the meta-carbon atom and the side chain carbon-atom to be connected by one electron. This means that the change



is very improbable.



Thus

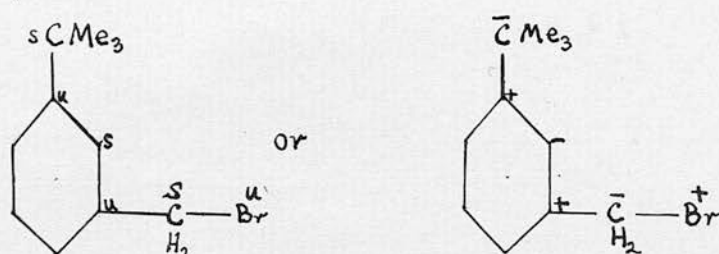
if this is the explanation of the slower hydrolysis of the meta-compound, the general influence is the only factor affecting the meta position.

(2)/

LG

(2) Octet stability.

A depressing of the reactivity may be due however to another cause of alternation, such as electronic octet stability which would also account for the slower rate of reactivity of the meta-compound by reason of an unstable octet round the bromine atom, that is,



Here again either mechanism of production of alternation would explain the phenomena of the different rates of hydrolysis. The value of the alternating effect on the hydrolyses at 60° , calculated from the formula,

$$a = \frac{1}{2}(\log_{10} K_p - \log_{10} K_m),$$

where a is the magnitude of the alternating effect, K_p and K_m , the average velocity constants (vide Shoesmith and Slater, J.C.S., 1926, 215) is 0.13, compared with ^{the} value 0.28 for the methyl-group.

That the rate of hydrolysis of the benzyl bromide is very closely related to nuclear substitution, is borne out by the rule, first enunciated by Olivier, (Rev. /

(Rec.trav.chim.,1923,42,775).

"In a series of isomeric benzyl halides, those isomerides in which the $-CH_2Hal$ group is attached to the carbon atom of the benzene nucleus which is attacked during substitution of the corresponding benzene derivative are the ones from which the halogen is most readily removed by the hydrolysing agent."

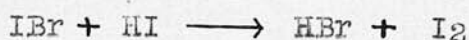
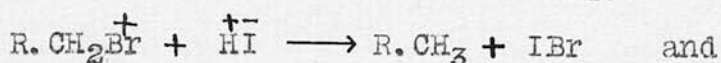
(quoted from Shoesmith and Taylor, J.C.S., 1926, 2832).

This rule is substantiated in the present instance.

(b) Reduction of m- and p-tertiary-butyl-benzyl bromides

It appears however that there is a factor at work, other than the electronic shift. This causes a "positivity" of the bromine atom, because the order of ease of removal of the bromine with hydrogen iodide in m- and p-tertiary-butyl-benzyl bromides is very definitely meta > para. The velocity of this reaction, the removal of "positive" bromine, must be influenced by a factor which increases the "positive" nature of the bromine. As has been seen before the electron shift mechanism does not appear adequate to bring this about and this is the only case in the present investigation where such a change cannot be regarded as the cause of increased activation of the bromine atom. Octet stability on the other hand fully explains the phenomenon. It may be however that the simple interpretation of the reduction/

reduction of this and similar compounds with hydrogen iodide is not correct and that the equations

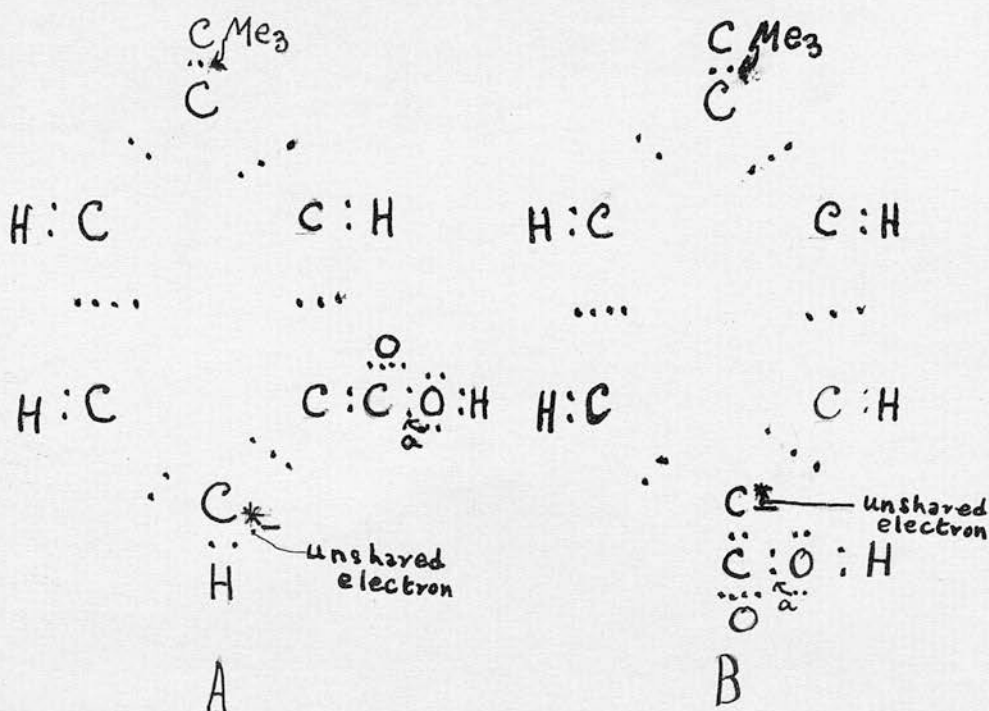


only approximately represent the reactions which are taking place.

The value of the alternating effect (a) in the reduction experiments, calculated from the equation as before at 110° is -0.07 , compared with -0.19 at 110° for the methyl-group [calculated from observations by Shoesmith and Slater (J.C.S., 1927, 1771)]. The effect is small but definite.

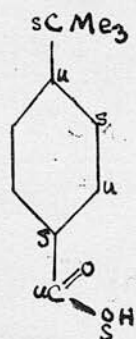
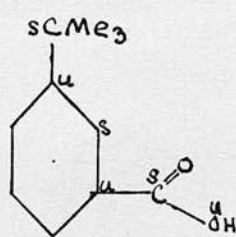
(c) Dissociation constants of m- and p-tertiary-butyl-benzoic acids.

The presence of an alternating influence is to be recognised here, since the para is the weaker acid, that is $K_p = 4.2 \times 10^{-3}$ and $K_m = 5.2 \times 10^{-3}$ at 25° . The electronic interpretation of such observations is as follows. Ionisation, according to Robinson, is due to the fundamental shift of electrons from the oxygen in the hydroxyl of the carboxyl-group towards the carbon atom. The meta- and para-compounds are therefore in the condition denoted by the two formulae A and B.



The para-carbon atom of the para-isomeride, since it is negatively charged, resists the process (a), that is, ionisation is depressed. The meta-carbon atom is not affected by process (a), only a general influence being really effective at this point and ionisation is not depressed so much as in the para-isomeride.

A difficulty arises when the dissociation constants are considered in the light of the theory of octet stability. In these cases, it would be expected that the octet round the oxygen atom, attached to the ionisable hydrogen would be stable in the para- and unstable in the meta-isomeride.



This means that the para- should be the stronger acid, which is the reverse of the experimental evidence. In this connection, therefore, it appears as if an examination of the transmission of influences through atoms, other than carbon, would be a valuable field of inquiry.

STERIC EFFECT.

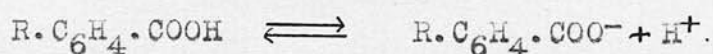
The inhibiting manner in which reactivity is affected by the steric influence of the tertiary-butyl-group, due to the space the group occupies, has been remarked upon from time to time in the thesis. The introduction of a nitro-group or bromine atom into the ortho-position is an operation difficult to perform and it is necessary to place a nitro-group in the para-position, in order to prepare compounds from which ortho-substituted derivatives may then be obtained. Even then, substitution is slower than in the corresponding toluene derivatives. The steric influence can therefore be counteracted, a fact which is borne out in the case of reduction of o-iodo-tertiary-butyl-benzene, already described.

Abnormality of o-tertiary-butyl-benzoic acid.

The dissociation constant of o-tertiary-butyl-benzoic acid ($K_{0.25} = 2.8 \times 10^{-2}$) is abnormally high (compare/

(compare $K_{m_{25^\circ}} = 5.2 \times 10^{-3}$ and $K_{p_{25^\circ}} = 4.2 \times 10^{-3}$).

This may be accounted for on the basis of the theory of Flürscheim (loc.cit. p.725) who says that the great acidity of ortho-substituted acids is due to the steric influence of the substituent group which disturbs the normal equilibrium between dissociated and non-dissociated molecules in the direction of the upper arrow in the equation:



This is because the proximity of the substituent to the carboxyl-group prevents recombination of the hydrogen ion and the anion $R.C_6H_4.CO_2^-$ to a greater extent than in the meta- and para-compounds and hence ortho-substituted acids have an exceptionally high dissociation constant. The acid is also remarkable in two other instances, namely, (1) its low melting point and (2) its high solubility in water as compared with the other isomerides. A comparison of the melting points (A) and solubilities in water at 25° (B) of the three isomeric tertiary-butyl-benzoic acids (x) and the toluic acids (y) is given in Table XI.

Table XI.

Isomeride	A		B	
	x	y	Concentration of a saturated solution of acid at 25° .	
	x	y	x	y
ortho	68°	104°	N/96	N/115*
meta	127°	110°	N/2246	N/139*
para	164°	179°	N/3646	N/394*

* Paul, Z.physikal.Chem., 1894, 14, 111.

CONCLUSION.

When transmitted through a benzene nucleus, the influence of the tertiary-butyl-group on atoms, either in combination with the nucleus or removed from it by a single carbon atom is similar to that of the methyl-group. The steric effect due to the former group is larger and the general and alternating effects less than those due to the latter. Whilst the effects of the general and steric influences are readily explicable (save in the case of reduction of *m*- and *p*-tertiary-butyl-benzyl bromides) it is seen that neither of the main theories put forward to account for the origin of the alternating influence explain the whole of the facts. The theory of electronic shift would not predict the difference between ease of reduction of *m*- and *p*-tertiary-butyl-benzyl bromides and the theory of octet stability the difference between the dissociation constants of *m*- and *p*-tertiary-butyl-benzoic acids.
